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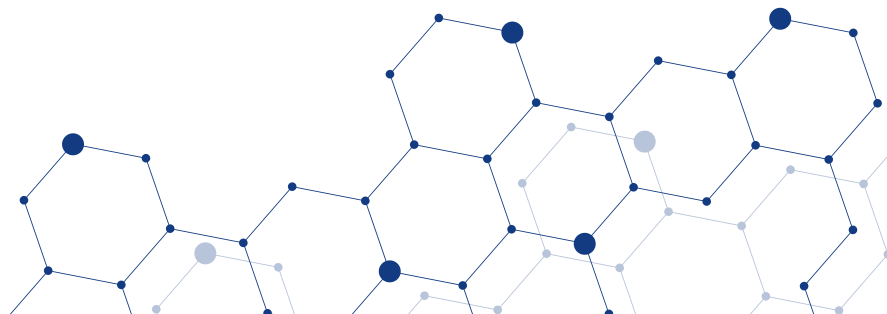
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NÍLZIO ANTÔNIO DA SILVA
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CLINICAL FACTORS ASSOCIATED WITH DEATH AND RECURRENCE IN INVASIVE BREAST CARCINOMA PATIENTS: PENALIZED LOGISTIC REGRESSION ANALYSIS IN A HOSPITAL COHORT

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ABSTRACT

Introduction: Identifying clinical predictors of death and recurrence in breast cancer is essential for prognostic stratification and individualized treatment. In cohorts with few events, conventional statistical methods are inadequate, requiring penalized approaches such as Firth's regression. **Objective:** To identify clinical factors associated with death and tumor recurrence in patients with invasive breast carcinoma in a hospital cohort, using Firth's penalized logistic regression. **Methods:** Retrospective cohort study with 97 patients with confirmed invasive breast carcinoma, excluding ductal carcinoma in situ. Univariate analysis used Fisher's exact test. Firth's penalized logistic regression models were fitted for death and recurrence, expressed as odds ratios (OR) with 95% CI. Event concentration by subgroup was presented in a staging $\times$ T-component cross-table. **Results:** Six deaths (6.2%) and 9 recurrences (9.3%) were recorded. Advanced staging (III–IV) was strongly associated with death (OR = 57.67; 95%CI: 9.39–643.91; $p < 0.001$) and recurrence (OR = 73.29; 95%CI: 14.05–544.21; $p < 0.001$). T3–T4 component showed associations of similar magnitude. In a multivariable model for recurrence, staging III–IV maintained independent association (adjusted OR = 39.99; 95%CI: 7.41–290.74; $p < 0.001$) after adjustment for axillary approach and HER2. Patients with stage III–IV and T3–T4 tumors had death rates of 50% and recurrence rates of 70%. The adjusted model ROC curve reached AUC = 0.942. **Conclusion:** Advanced clinical staging and T3–T4 component are fundamental determinants of adverse prognosis in invasive breast carcinoma. Firth's penalized logistic regression proved appropriate for analyzing rare outcomes in small cohorts.

Keywords: Breast neoplasms, Neoplasm recurrence, Local, Prognosis, Logistic regression, Survival analysis.

INTRODUCTION

Breast cancer represents the most common malignant neoplasm among women in Brazil and worldwide, with a significant impact on female morbidity and mortality. The prognosis of the disease is multifactorial, being determined by clinical, histological, and molecular characteristics

of the tumor, in addition to the extent of the disease at diagnosis. Early identification of factors associated with death and recurrence is essential for risk stratification, individualization of therapeutic strategies, and appropriate clinical follow-up.¹

From an epidemiological perspective, clinical stage at diagnosis is recognized as the main predictor of overall survival in breast cancer. Patients diagnosed at early stages (I-II) have five-year survival rates close to 90%, while those with locally advanced (III) or metastatic (IV) disease have substantially worse prognoses. In addition to staging, factors such as tumor size, axillary lymph node involvement, histological grade, and molecular profile — especially the triple-negative subtype — are independent predictors of recurrence and mortality widely documented in the literature.²

Conducting robust inferential analyses in small hospital cohorts poses relevant methodological challenges. When the number of observed events is low, estimates obtained by conventional logistic regression are susceptible to complete or quasi-complete separation bias, with consequent instability of the coefficients and excessively wide confidence intervals. In these situations, Firth penalized logistic regression is recommended because of its ability to produce unbiased estimates even in the presence of data separation, being particularly suitable for studies with few events per covariate.³

The present study aimed to identify clinical factors associated with death and tumor recurrence in patients with invasive breast carcinoma followed in a hospital cohort, using statistical methods appropriate for samples with a low number of events.⁴

METHODS

Study Design and Population

A retrospective observational cohort study was conducted at a private referral hospital for oncology in the state of Goiás, in the Central-West region of Brazil. Patients with a histologically confirmed diagnosis of invasive breast carcinoma were included. The following were excluded: (1) cases of ductal carcinoma in situ (DCIS, stage 0), as they do not represent invasive disease; (2) patients with missing essential clinical data. The final sample consisted of 97 patients.

Variables and Outcomes

The primary outcomes were death from any cause and tumor recurrence (local, regional, or distant), both treated as binary variables. The explanatory variables included: clinical stage (I-II vs. III-IV), T component of the TNM classification (T1-T2 vs. T3-T4), histological type (IDC, ILC, inflammatory carcinoma, and others), tumor grade (G1 vs. G2-G3), axillary status (negative vs. positive), molecular profile (HR-positive, HER2-positive, triple-negative subtype), and treatment modalities performed (chemotherapy, hormone therapy, and radiotherapy).

Statistical Analysis

Descriptive analysis was performed using absolute and relative frequencies for categorical variables. Univariate analysis used Fisher's exact test to assess the association between clinical variables and the outcomes, due to the small number of events. Variables with a statistically significant association or potential clinical relevance were included in the regression models.

Firth penalized logistic regression models were fitted for both outcomes. This method reduces estimation bias in situations of complete or quasi-complete separation of the data, a common condition in datasets with few events. Results were expressed as odds ratios (ORs) with 95% confidence intervals

(95% CIs). In an exploratory multivariable model for recurrence, stage, axillary status, and HER2 status were included as covariates. The discriminatory ability of the models was assessed by the area under the ROC curve (AUC). All analyses were performed using R software (version 4.x; R Foundation for Statistical Computing, Vienna, Austria), with a significance level of 5%.

RESULTS

Sample Characteristics

A total of 97 patients with invasive breast carcinoma were included, after the exclusion of 2 cases of DCIS. During follow-up, 6 deaths (6.2%) and 9 recurrences (9.3%) were recorded. The clinical characteristics of the sample are presented in Table 1.

Table 1 : Clinicopathological characteristics of the sample (n = 97).

Variable	n	%
Clinical Stage		
I-II	87	89.7
III-IV	10	10.3
T component (TNM)		
T1-T2	86	88.7
T3-T4	11	11.3
Histological type		
Invasive ductal carcinoma (IDC)	80	82.5
Invasive lobular carcinoma (ILC)	7	7.2
Inflammatory carcinoma	2	2.1
Other subtypes	8	8.2
Tumor grade		
G1	14	14.4
G2	69	71.1
G3	14	14.4
Axillary approach		
Negative	69	71.1
Positive	28	28.9
Molecular profile		
HR-positive (ER or PR)	75	77.3
HER2-positive	19	19.6
Triple-negative subtype	15	15.5
Treatments performed		
Chemotherapy	56	57.7
Neoadjuvant	32	33.0
Adjuvant	22	22.7
Hormone therapy	74	76.3
Radiotherapy	75	77.3
Outcomes		
Death	6	6.2
Recurrence	9	9.3

IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; HR: hormone receptors.

Univariate Analysis — Fisher's Exact Test

In the univariate analysis for the outcome of death (Table 2), a statistically significant association was observed with variables related to tumor extent: TNM risk, N component, clinical stage, T component, and hormone therapy (all $p < 0.001$), as well as chemotherapy ($p = 0.036$) and tumor grade ($p = 0.043$). Axillary status ($p = 0.052$) and histological type ($p = 0.083$) showed borderline associations.

Table 2 : Fisher's exact test — association between clinical variables and death (n = 97).

Variable	N	p-value
TNM risk	97	< 0.001
TNM N component	97	< 0.001
Clinical stage	97	< 0.001
TNM T component	97	< 0.001
Hormone therapy	97	< 0.001
Chemotherapy	97	0.036
Tumor grade	97	0.043
Axillary approach	97	0.052
Histological type	97	0.083
Reconstruction	97	0.481
Radiotherapy	97	0.621
Educational level	97	0.679
Family history	97	1.000
HER2	97	1.000

For the outcome of recurrence (Table 3), significant associations included the N component, TNM risk, clinical stage, T component, hormone therapy, chemotherapy, and axillary status. HER2 showed a borderline association ($p = 0.066$).

Table 3: Fisher's exact test — association between clinical variables and recurrence (n = 97).

Variable	N	p-value
TNM N component	97	< 0.001
TNM risk	97	< 0.001
Clinical stage	97	< 0.001
TNM T component	97	< 0.001
Hormone therapy	97	< 0.001
Chemotherapy	97	0.009
Axillary approach	97	0.014
HER2	97	0.066
Tumor grade	97	0.135
Educational level	97	0.161
Histological type	97	0.368
Radiotherapy	97	0.430
Reconstruction	97	1.000
Family history	97	1.000

Firth Penalized Logistic Regression — Univariate Models

The univariate Firth models (Table 4) showed a strong association of stage III-IV with death (OR = 57.67; 95% CI: 9.39–643.91; $p < 0.001$) and recurrence (OR = 73.29; 95% CI: 14.05–544.21; $p < 0.001$).

The T3–T4 component showed associations of similar magnitude for both outcomes (death: OR = 49.36; 95% CI: 8.24–539.63; $p < 0.001$; recurrence: OR = 57.67; 95% CI: 11.70–395.81; $p < 0.001$). Regarding histological type, the “Other” group (vs. IDC) was significantly associated with death (OR = 8.16; 95% CI: 1.53–44.22; $p = 0.016$), whereas ILC showed no significant difference for either outcome. The wide confidence intervals reflect the small number of events.

Table 4: Firth Penalized Logistic Regression — Univariate Models for Death and Recurrence.

Model	Comparison	OR (95% CI)	p-value
Outcome: Death			
Clinical stage	III–IV vs I–II	57.67 (9.39–643.91)	< 0.001
T component	T3–T4 vs T1–T2	49.36 (8.24–539.63)	< 0.001
Histological type	ILC vs IDC	1.48 (0.01–17.56)	0.811
Histological type	Other vs IDC	8.16 (1.53–44.22)	0.016
Outcome: Recurrence			
Clinical stage	III–IV vs I–II	73.29 (14.05–544.21)	< 0.001
T component	T3–T4 vs T1–T2	57.67 (11.70–395.81)	< 0.001
Histological type	ILC vs IDC	0.76 (0.01–7.66)	0.854
Histological type	Other vs IDC	4.22 (0.88–17.90)	0.069

IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; OR: odds ratio; 95% CI: 95% confidence interval.

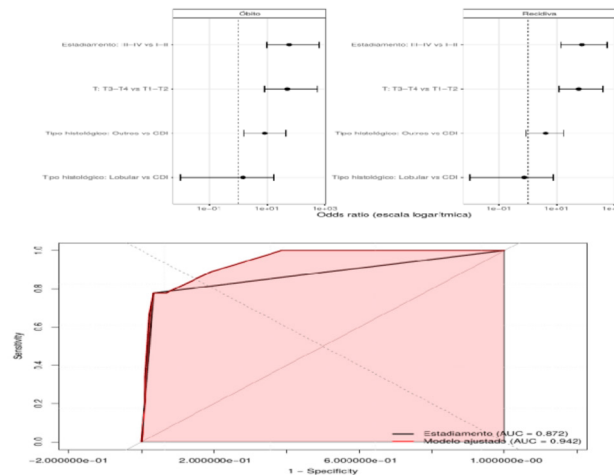


Figure 1: Forest plot of Firth penalized logistic regression models for the outcomes of death and recurrence (upper panel), and ROC curves comparing the model with clinical stage alone (AUC = 0.872) versus the model adjusted for clinical stage, axillary approach, and HER2 (AUC = 0.942; lower panel). The dashed line indicates OR = 1.

Exploratory Multivariable Model for Recurrence

In the multivariable model for recurrence (Table 5), stage III–IV remained strongly associated with

the outcome after adjustment for axillary approach and HER2 status (adjusted OR = 39.99; 95% CI: 7.41–290.74; $p < 0.001$). Positive axillary approach (OR = 2.01; 95% CI: 0.27–12.74; $p = 0.467$) and HER2-positive status (OR = 2.62; 95% CI: 0.35–19.21; $p = 0.335$) did not show statistically significant independent associations after adjustment.

Table 5: Exploratory Multivariable Model (Firth Regression) — Predictors of Recurrence.

Variable	Adjusted OR (95% CI)	p-value
Clinical stage III–IV vs. I–II	39.99 (7.41–290.74)	< 0.001
Positive axillary approach	2.01 (0.27–12.74)	0.467
HER2-positive status	2.62 (0.35–19.21)	0.335

OR: adjusted odds ratio; 95% CI: 95% confidence interval.

Concentration of Events by Subgroup

Table 6 and Figure 2 present the distribution of death and recurrence according to the main clinical subgroups. Patients with stage III–IV disease and T3–T4 tumors had death and recurrence proportions of 50% (5/10) and 70% (7/10), respectively, compared with less than 2% for both outcomes among patients with early-stage disease (stage I–II, T1–T2). The concentration of events in the triple-negative subgroup was also substantial — 26.7% for deaths and 33.3% for recurrences, versus 2.4% and 4.9%, respectively, in the other subgroups.

Table 6: Proportion of Death and Recurrence According to Clinical Subgroups (n = 97).

Subgroup	n	Deaths n (%)	Recurrences n (%)	p-value*
Stage I–II	87	1 (1.1)	2 (2.3)	< 0.001
Stage III–IV	10	5 (50.0)	7 (70.0)	< 0.001
T1–T2	86	1 (1.2)	2 (2.3)	< 0.001
T3–T4	11	5 (45.5)	6 (54.5)	< 0.001
Negative axilla	69	1 (1.4)	2 (2.9)	0.052 / 0.014
Positive axilla	28	5 (17.9)	7 (25.0)	0.052 / 0.014
Triple-negative — No	82	2 (2.4)	4 (4.9)	< 0.001
Triple-negative — Yes	15	4 (26.7)	5 (33.3)	< 0.001

*p-value by Fisher's exact test; values separated by a slash correspond to the p-value for death / p-value for recurrence, respectively.

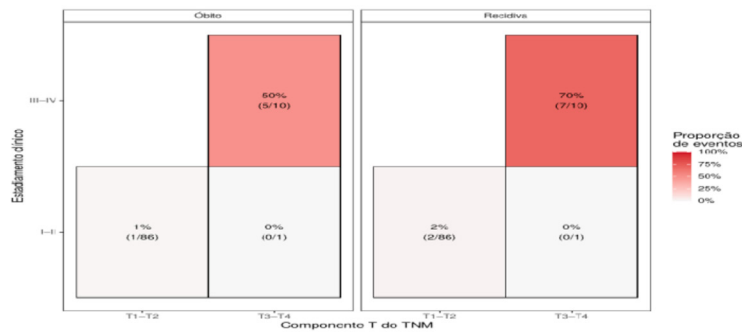


Figure 2: Proportion of death and recurrence according to clinical stage and the T component of the TNM system. The values in each cell represent the proportion of events in the corresponding subgroup. A clear concentration of events was observed among patients with stage III-IV disease and T3-T4 tumors.

DISCUSSION

The results of this study confirm the central role of clinical stage as the main prognostic determinant in invasive breast carcinoma, with associations of large magnitude for both death and recurrence, which were maintained after multivariable adjustment. Patients with stage III-IV disease had approximately 58- and 73-fold higher odds of death and recurrence, respectively, compared with patients with stage I-II disease — a finding consistent with the established oncology literature and biologically plausible, given the greater tumor burden and therapeutic limitations inherent to advanced disease.⁵

The T component of the TNM system showed associations of similar magnitude to overall stage, which is expected given the strong correlation between these two parameters. T3-T4 tumors, due to their greater tumor volume and higher probability of lymph node involvement and distant spread, are associated with poorer locoregional control and a higher risk of systemic recurrence. Cross-analysis of clinical stage × T component revealed that adverse events were specifically concentrated in the subgroup with both unfavorable factors: proportions of 50% for death and 70% for recurrence among patients with stage III-IV disease and T3-T4 tumors.⁶

The “Other” histological subtype showed a significant association with death (OR = 8.16; $p = 0.016$), a result that warrants careful interpretation. This group is heterogeneous and includes Paget and medullary carcinomas — subtypes with distinct prognoses. The wide confidence intervals observed in the estimates for histological type reflect both the small number of events and the within-group biological heterogeneity, limiting definitive conclusions.⁷

In the exploratory multivariable model for recurrence, stage III-IV remained independently associated with the outcome after adjustment for axillary approach and HER2 status. The lack of statistical significance for positive axillary approach and HER2 in the adjusted model does not imply a lack of clinical relevance of these factors, but rather reflects the limited statistical power of this sample. With only 9 recurrence events, the model's ability to detect independent effects of additional covariates is substantially reduced.⁸

The adjusted model achieved an AUC of 0.942 for predicting recurrence, suggesting excellent discriminatory ability. However, this value should be interpreted with caution: in small samples with

a low number of events, the AUC tends to be overestimated, and external validation of the model would be necessary before any clinical application. The improvement in AUC from 0.872 (model with clinical stage alone) to 0.942 (adjusted model) indicates that the inclusion of additional covariates adds discriminatory value, although again subject to the limitations of the sample context.⁹

From a methodological perspective, the use of Firth penalized logistic regression was appropriate for the context of this study. The quasi-complete separation of the data — resulting from the strong association between advanced stage and the occurrence of events in a sample with few cases — would render conventional logistic regression estimates unstable or even incalculable. The Firth method addresses this problem by introducing a penalty into the likelihood function, producing estimates with reduced bias even in situations of separation.

The main limitations of the study are the small sample size and the low number of events, which impose restrictions on statistical power and the stability of multivariable estimates. The retrospective nature of the study and its single-center setting limit the generalizability of the findings. Prospective studies with larger series and prolonged follow-up are needed to confirm the identified associations and to develop prognostic models with external validation.¹⁰

CONCLUSION

O estadiamento clínico avançado (III-IV) e o componente tumoral T3-T4 constituíram os principais determinantes do prognóstico adverso nesta coorte de pacientes com carcinoma mamário invasivo, associando-se independentemente a maiores riscos de óbito e recidiva tumoral. A regressão logística penalizada de Firth mostrou-se abordagem estatisticamente adequada para o estudo de desfechos raros em séries clínicas de pequeno porte, permitindo estimativas estáveis na presença de separação quase completa dos dados.

Os achados reforçam a relevância do diagnóstico precoce e do estadiamento preciso como ferramentas fundamentais para a estratificação prognóstica e orientação das decisões terapêuticas em oncologia mamária. A ampliação da casuística e o seguimento prolongado de séries institucionais são necessários para a consolidação de modelos prognósticos validados e aplicáveis à realidade clínica regional.

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PREDICTING THE 2026–2027 WHOOPING COUGH TREND IN BRAZIL BASED ON ARIMA AND SARIMA MODELS

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ABSTRACT

Introduction: Although the introduction of vaccination against whooping cough significantly reduced its incidence, recent years have shown a resurgence, emphasizing the importance of temporal and regional analyses to understand disease dynamics and support epidemiological surveillance. **Objective:** To develop a time series model to forecast whooping cough cases in Brazil for the years 2026 and 2027. **Material and Methods:** This ecological time series study analyzed whooping cough notifications in Brazil from 2007 to 2024 using publicly available data from SINAN/Tabnet/DataSUS. Data were organized into monthly and annual series following GATHER guidelines. Series characteristics were evaluated using Dickey-Fuller, Mann-Kendall, Kruskal-Wallis, and Box-Pierce tests. ARIMA and SARIMA models were applied to forecast cases for 2026 and 2027 with 95% confidence intervals. Analyses were performed using R (v4.3.2) and Excel, according to established protocols previously. **Results:** Between 2007 and 2024, 42354 cases were recorded of whooping cough. It was observed that the South and Southeast were the regions most affected by whooping cough during this period. The results indicated that, although the ARIMA and SARIMA models identified for each region exhibited relatively stable profiles of stationarity, trend, and seasonality, the analysis based on the model adjusted with the complete dataset up to 2024 allowed for more robust and reliable forecasts. The forecast indicates an increase in whooping cough cases in the Southeast region from May to October 2026 and from July to December 2027. In the South region, a smaller but prolonged increase is observed from January and March 2026 and from August 2026 to December 2027, suggesting significant seasonal variations. **Conclusion:** Whooping cough is reemerging in Brazil with cyclical trends and unequal geographic

distribution. Forecasts suggest increasing cases in the coming years, especially in the Southeast and South, reinforcing the need for continuous surveillance, targeted vaccination campaigns, and proactive public health interventions.

Keywords: ARIMA, Brazil, SARIMA, TSM, Whooping cough.

INTRODUCTION

Whooping Whooping cough, also known as *pertussis*, is an acute respiratory infection caused by the Gram-Negative bacterium *Bordetella pertussis*. This disease is highly contagious being transmitted through direct contact with respiratory droplets expelled by infected individuals when they cough, sneeze, or speak. The disease is clinically characterized by intense paroxysmal coughing followed by a high-pitched inspiratory “whoop” or post-tussive vomiting. In severe cases, symptoms may progress for apnea, hypoxia, seizures, pneumonia, encephalopathy, and until death.¹⁻³ The diagnostic is realized for through microbiological identification (culture), PCR and/or serology, but delayed diagnosis is common due to the overlap of symptoms with other respiratory conditions.^{1,2}

Vaccination remains the cornerstone of prevention and it consists of primary immunization (infancy) with DTaP, followed by booster doses in adolescence. Some studies, they also propose the vaccination during the phase adulthood.⁴ Immunization during pregnancy is particularly recommended to protect newborns through passive antibody transfer.⁴⁻⁶

Despite the availability of the vaccine, short-lived immunity combined with low adherence to immunization programs complete in some countries, contribute to the occurrence of periodic outbreaks.^{7,8} These factors enhance the cyclic nature of whooping cough incidence, which recur every 3 to 5 years, regardless of the type of immunization or vaccination coverage.⁹

Other factors may also play a role important in these outbreaks, such as the introduction, in various countries, of the acellular vaccine replacing the attenuated vaccine, the phenotypic variability of *B. pertussis*, and the increasing resistance bacterial to commonly used antibiotics, especially macrolides.¹⁰ These outbreaks primarily affect unvaccinated individuals, particularly infants, posing significant health risks during early childhood.⁴

The resurgence of whooping cough cases in recent years underscores its ongoing importance as a public health concern globally (11). Among the countries of South America, Brazil stands out for the resurgence of whooping cough, with a marked peak starting in 2024. This scenario can indicate the beginning of a new epidemic cycle, particularly in the Southeast and South regions, and highlights regional disparities.¹² Thus, the epidemiological vigilance, especially during epidemic peaks, is fundamental to improving outcomes and to assist in the health decision-making process.^{1,2}

The application of time series modeling (TSM) has become increasingly relevant in epidemiological surveillance of various diseases.¹³⁻¹⁶ The ARIMA/SARIMA models allow for the identification of temporal patterns, seasonality, and regional disparities.¹³⁻¹⁶ These approaches enhance the ability to project future trends with statistical reliability.^{17,18} Predictive modeling based on historical data helps identify high-risk periods and regions and strengthens decision-making processes in public health for optimizing resource allocation, vaccination campaigns. Moreover, outbreak prediction supports faster responses to emerging outbreaks.¹⁴

This study had with aims, using time series modeling, to forecast case of whooping cough counts for 2026, and 2027. These projections aim to support proactive planning in surveillance,

prevention efforts and more effective epidemic management strategies.

MATERIAL AND METHODS

Ethical Aspects

The data analyzed of whooping cough in this study were obtained from the Information System for Notifiable Diseases (SINAN), a publicly accessible and unrestricted database provided by SINAN via Tabnet/DataSUS.¹⁹ According to Resolution No. 510/2016 of the National Health Council, studies using exclusively public data do not require approval by a Research Ethics Committee.²⁰ Furthermore, no individualized or sensitive information was accessed or disclosed.

Study design and context

This is an ecological study with a time series approach, conducted in accordance with the GATHER guidelines.²¹ Whooping cough notifications in Brazil from 2007 to 2024 were analyzed. The data were obtained from SINAN through the platform Tabnet / DataSUS which consolidates the mandatory notifications of whooping cough made within 24 hours after suspicion, as established by Consolidation Ordinance No. 4, dated September 28, 2017 can be accessed at: <http://tabnet.datasus.gov.br/cgi/defthtm.exe?sinanet/cnv/coquebr.def>.²²

Brazil was selected as the study area due to the availability of data and the epidemiological significance of whooping cough at the national level. The data, sourced from SINAN, were initially organized in annual spreadsheets and subsequently consolidated into a single database. A rigorous data quality control procedure was conducted to identify inconsistencies, missing values, and ensure overall data integrity. The consolidated dataset was used for model development. The methodology is summarized in the flowchart presented in Figure 1.

Statistical analysis and predictions of Whooping Cough for 2026 and 2027

The data were organized into monthly and annual time series for statistical analysis. Preliminary assessments were conducted to examine the characteristics of the time series using the following hypothesis tests: Dickey-Fuller test (stationarity), Mann-Kendall test (trend), Kruskal-Wallis test (seasonality), and Box-Pierce test (residual autocorrelation).

Based on the results of these tests, the data were modeled using ARIMA and SARIMA approaches. The best model was used to forecast whooping cough cases for the years 2025, as well as 2026 and 2027. Although 2025 is the current year, predictive modeling was necessary due to the unavailability of confirmed data at the time of analysis. This preliminary forecast enabled the extension of projections to 2026 and 2027. Estimates were generated using point and interval statistical inference, with a 95% confidence interval to enhance the robustness of the predictions. All analyses were conducted using Microsoft Excel 2020 and R software (version 4.3.2) for statistical processing and model development.²³ The methodology applied follows the time series simulation protocol previously outlined.^{14, 24}

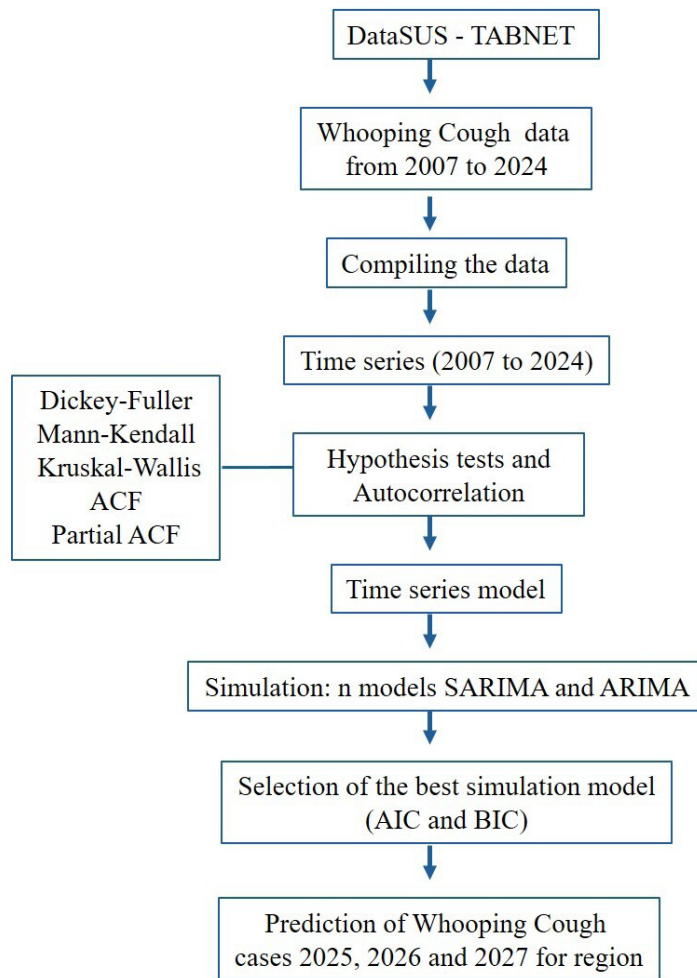


Figure 1 : Flowchart representing the methodology used in this study. SARIMA: Seasonal Auto-Regressive Integrated Moving Average Model; ARIMA: Auto-Regressive Integrated Moving Average Model; ACF: Autocorrelation Function; AIC: Akaike Information Criterion; BIC: Bayesian Information Criterion.

RESULTS

In the SINAN/ Tabnet/ DataSUS database, 18 dataframes were identified containing a total of 42354 whooping cough notifications in Brazil, from 2007 to 2024. All these notifications of whooping cough of DataSUS were included in the study. The total number of whooping cough cases recorded in the SINAN/Tabnet/DataSUS database between 2007 and 2024 are described in the Table 1.

Table 1 : Total number of whooping cough cases in the SINAN/Tabnet/DataSUS (2007 for 2024).

Year	Case
2007	781
2008	1309
2009	1131
2010	548
2011	2034
2012	5137
2013	6451
2014	8603
2015	3321
2016	1318
2017	1759
2018	2237
2019	1615
2020	302
2021	154
2022	246
2023	207
2024	5201
Total	42354

The total number and relative frequency of whooping cough cases by region are presented in Table 2. The total number of cases of whooping cough by year and region is detailed in the supplementary Table 1.

Table 2 : Total number and relative frequency of whooping cough cases by região (2007 for 2024).

Region	Case	Frequency relative (%)
Central-West	2901	6,85
North	2569	6,07
North East	9203	21,73
South	10308	24,34
Southeast	17373	41,02
Total	42354	100

Between 2020 and 2023, the world faced the COVID-19 pandemic, a period marked by a substantial reduction in whooping cough cases, followed by a significant increase in 2024. In this context, a preliminary analysis was conducted using the AIC (Akaike Information Criterion) and BIC (Bayesian Information Criterion) information criteria, as well as hypothesis tests, to compare the models built with data up to 2019 and those that included data up to 2024. In total, 233 models were generated using data up to 2019 and 232 models using data up to 2024. The AIC and BIC values for each model are detailed in Supplementary Table 2.

The AIC and BIC parameters indicate that the best model generated for 2019 showed higher quality than the best model generated for the dataset up to 2024. All AIC and BIC parameters of the best models generated for 2019 and 2024 are presented in Table 3.

Table 3 : Parameters of the hypothesis tests and models applied to the datasets up to 2019 and 2024.

Region	Year	Models	AIC	BIC	Dickey-Fuller	Mann-Kendall	Kruskal-Wallis
North	2024	ARIMA(3,1,2)	1533,65	1553,88	0,01	0,00	0,58
	2019	SARIMA(3,2,3)(3,2,3)	1072,23	1109,51	0,02	0,02	0,02
North East	2024	ARIMA(3,1,2)	1926,60	1946,82	0,28	0,01	0,99
	2019	ARIMA(3,1,2)	1435,47	1453,73	0,35	0,00	0,99
Southeast	2024	ARIMA(3,1,2)	2209,87	2230,09	0,18	0,00	0,98
	2019	ARIMA(3,2,3)	1597,48	1618,74	0,56	0,01	0,49
Central-West	2024	ARIMA(3,1,2)	1538,22	1558,44	0,29	0,00	0,99
	2019	ARIMA(3,1,2)	1117,19	1135,45	0,60	0,00	0,99
South	2024	ARIMA(2,0,3)	2182,81	2206,44	0,46	0,00	0,91
	2019	ARIMA(1,1,1)	1407,58	1416,71	0,55	0,05	0,25

Additionally, the application of hypothesis tests indicated that the ARIMA (3,1,2) models for the Northeast and Central-West regions showed similar parameters for both the dataset up to 2019 and the dataset up to 2024, maintaining the same stationarity (Dickey-Fuller), trend (Mann-Kendall), and seasonality (Kruskal-Wallis) profiles (Table 3).

For the South region, the model identified for the dataset up to 2019 and since 2024 was ARIMA (1,1,1) and ARIMA (2,0,3), respectively. The parameters obtained from the hypothesis tests indicate that the profiles of stationarity (Dickey-Fuller: 2019 = 0.55; 2024 = 0.46), trend (Mann-Kendall: 2019 = 0.05; 2024 = 0.00), and seasonality (Kruskal-Wallis: 2019 = 0.25; 2024 = 0.91) remain similar (Table 3).

For the Southeast region, the model identified for the dataset up to 2019 was ARIMA (3,1,2), and for the dataset up to 2024, it was ARIMA (3,2,3). The parameters obtained from the hypothesis tests indicate that the profiles of stationarity (Dickey-Fuller: 2019 = 0.56; 2024 = 0.18), trend (Mann-Kendall: 2019 = 0.01; 2024 = 0.00), and seasonality (Kruskal-Wallis: 2019 = 0.49; 2024 = 0.98) remain similar (Table 3).

For the North region, the model identified for the dataset up to 2019 was SARIMA (3,2,3)(3,2,3),

and for the dataset up to 2024, it was ARIMA (3,1,2). The hypothesis tests indicate that the profiles of stationarity (Dickey-Fuller: 2019 = 0.02; 2024 = 0.01) and trend (Mann-Kendall: 2019 = 0.02; 2024 = 0.00) are similar. However, the ARIMA (3,1,2) model for 2024 did not show evidence of seasonality (Kruskal-Wallis: 2024 = 0.58), whereas the SARIMA (3,2,3)(3,2,3) model for 2019 did show evidence of seasonality (Kruskal-Wallis: 2019 = 0.02) (Table 3).

Despite these findings, using the models based on the dataset up to 2019 could result in biased predictions for 2025, 2026, and 2027, due to the absence of five years of whooping cough notifications recorded in SINAN/Tabnet/DataSUS. Conversely, using the model estimated with higher AIC and BIC parameters would yield higher-quality predictions, owing to the larger amount of data. Therefore, the present study proceeded with the preliminary analysis considering the model generated from the dataset that included whooping cough data up to 2024.

Figure 2A presents the number of whooping cough cases in Brazil from 2007 to 2024, shown both on a monthly and annual basis, highlighting a marked decrease in cases between 2020 and 2023, followed by a substantial increase in 2024. Figure 2B provides the same data, also on a monthly and annual basis, disaggregated by region (North, Northeast, Southeast, South, and Central-West), allowing for a regional analysis of the disease's epidemiological dynamics. Between 2012 and 2014, a whooping cough outbreak was observed in the country, with the Southeast region standing out for having the highest number of reported cases. Furthermore, the pronounced increase in cases recorded in 2023 was primarily driven by a rise in notifications in the Northeast and Southeast regions. Figure 2C presents a heat map illustrating the distribution of whooping cough cases across the Brazilian regions from 2007 to 2024.

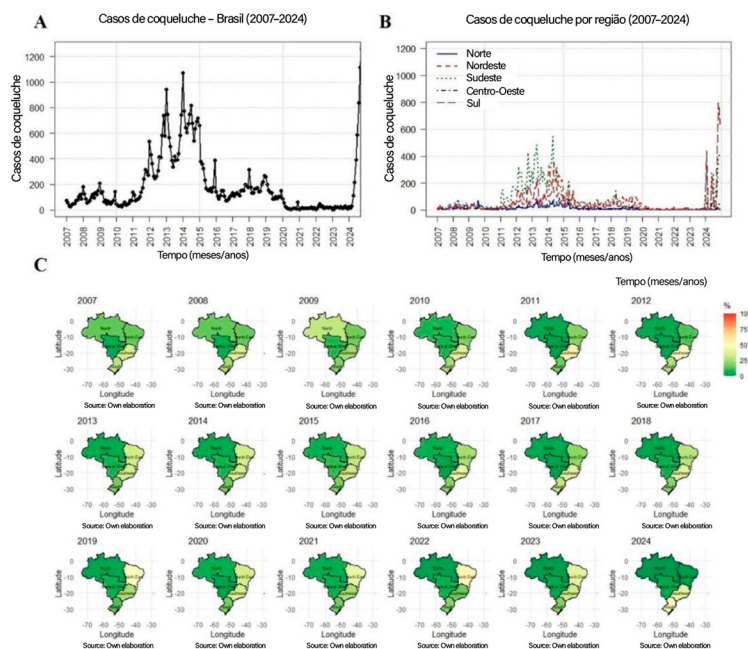


Figure 2 : A) Whooping Cough Cases in Brazil, 2007 for 2024; B) Whooping Cough Cases by Brazilian Region, 2007 for 2024; C) Heat map illustrating the distribution of whooping cough cases across the Brazilian regions from 2007 to 2024. In the map, the colors range from green to red, corresponding to the intensity of case numbers: darker green tones indicate a lower number of whooping cough cases, while lighter tones represent regions with a higher number of reported cases.

Figures 3A, 3B, and 3C present heat maps showing the predicted number of whooping cough cases by region for the years 2025, 2026, and 2027, respectively. The prediction for 2025 was included because, at the time of the analysis, data for that year were not yet available. Figure 3D illustrates the monthly predicted cases by region, highlighting an expected increase between May and October 2026 in the Southeast region. A similar pattern is projected for 2027, with a rise in cases anticipated between July and December in the same region. Additionally, an increase in reported cases is expected in the South region between December 2025 and February 2026, indicating significant seasonal variations, with a more gradual but prolonged increase projected from August 2026 to December 2027.

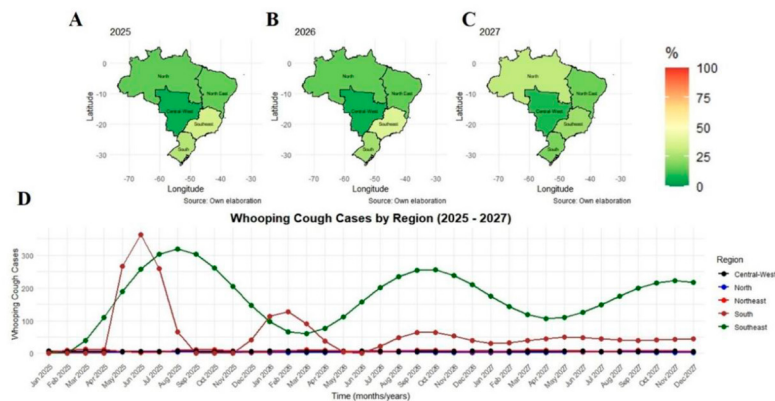


Figure 3 : A - C) Heat maps showing the predicted number of whooping cough cases by region for the years 2025, 2026, and 2027, respectively. In the map, the colors range from green to red, corresponding to the intensity of case numbers: darker green tones indicate a lower number of whooping cough cases, while lighter tones represent regions with a higher number of reported cases. D) Prediction of monthly whooping cough cases from 2025 to 2027, stratified by region.

DISCUSSION

The recent resurgence of whooping cough in countries such as China, the United States, Brazil, and Mexico has once again become a global public health concern, despite the availability of effective immunization.^{12,25,26} In parallel, the prediction of epidemiological scenarios has become established as a strategic tool for the surveillance of various diseases, including whooping cough.^{27,28} These predictions aim to provide more accurate information to support the optimization of financial resources, the appropriate allocation of human resources, and the public health decision-making process for addressing various diseases.²⁷

In the present study, data were obtained from SINAN/Tabnet/DataSUS, a public database managed by the Brazilian Ministry of Health, which compiles notifications of whooping cough cases reported since 2007 (29, 30). The analysis of 42354 notifications recorded between 2007 and 2024 enabled the assessment of the epidemiological dynamics of whooping cough in Brazil. This analysis reinforced the cyclical nature of the disease, with 3 to 5 years intervals, as previously reported by the Brazilian Ministry of Health and also observed in other populations worldwide.^{11, 29, 31}

Interestingly, in the present study, a marked increase in whooping cough notifications was observed in 2014, possibly resulting from the updated definitions of suspected and confirmed cases issued by the Brazilian Ministry of Health, which began to incorporate age-specific criteria and cough duration.³² This change made the Brazilian surveillance system more sensitive to case

detection, particularly among infants, who represent the group most affected by the disease. Additionally, this increase coincides with the final phase of the epidemic peak that began in Epidemiological Week (EW) 30 of 2011 and extended until EW 33 of 2014.^{32,33}

In the present study, the initial analyses indicated a marked reduction in whooping cough cases between 2020 and 2023, followed by a substantial increase in 2024. This pattern is similar to that observed in a study conducted in China, which reported a peak in whooping cough cases shortly after the COVID-19 pandemic.²⁵ In our study, we believe that the reduction in cases between 2020 and 2023, followed by the sharp increase in 2024, reflects the impacts of the COVID-19 pandemic on epidemiological surveillance, the decrease in whooping cough vaccination coverage, and the resumption of mobility and social interaction patterns.³⁴ Previous studies have reported that social distancing measures and the prioritization of COVID-19 vaccination contributed to a temporary reduction in the circulation of other respiratory pathogens, including *B. pertussis*.^{25,34} On the other hand, the increase observed in 2024 may reflect a rebound effect associated with the resumption of epidemiological surveillance, the reopening of schools and borders, and the low population immunity (herd immunity) following a prolonged period of reduced exposure to the infectious agent.²⁵

This recent study conducted by (2024) also reported a notable increase in whooping cough cases following the COVID-19 pandemic, with shifts in the affected age groups, a higher incidence among older children, increased vaccine hesitancy, and a greater prevalence of macrolide-resistant *B. pertussis* strains.³⁵ In our study, vaccine hesitancy and macrolide resistance were not assessed due to the absence of these variables in the SINAN/Tabnet/DataSUS databases.

In our study, the distribution of whooping cough cases by region from 2007 to 2024 showed a higher number of notifications in the Southeast, South, and Northeast regions, respectively. This pattern may be explained by several factors, including the higher population density and urban concentration in the Southeast and South regions, which can facilitate the transmission of highly contagious respiratory diseases such as whooping cough.³⁶ Furthermore, these regions have more structured surveillance systems with greater diagnostic capacity, which may result in higher case notification rates. The heterogeneity in whooping cough vaccination coverage, both among children and pregnant women, may also contribute to the presence of susceptible populations, particularly in areas of the Northeast where access to healthcare services is more limited.^{37,38} Other factors, such as population mobility and socioeconomic inequalities, may have further amplified transmission, contributing to the case peaks observed in these regions.

On the other hand, time series modeling based on SARIMA and ARIMA frameworks has been widely used to reflect incidence rates of various infectious diseases, including dengue, malaria, hepatitis E, among others (39-43). In our study, the model analysis showed that despite the alterations in case dynamics during the pandemic, the patterns of stationarity, trend, and seasonality remained similar for most regions when comparing the models constructed with data up to 2019 and those incorporating data up to 2024.

In the Northeast and Central-West regions, the ARIMA (3,1,2) models exhibited consistent parameters, indicating stability in the historical patterns of the disease even in the face of disruptions caused by the COVID-19 pandemic. In the South and Southeast regions, changes were observed in the model parameters, with the ARIMA (1,1,1) model shifting to ARIMA (2,0,3) in the South, and the ARIMA (3,1,2) model shifting to ARIMA (3,2,3) in the Southeast, respectively. These modifications suggest slight changes in trend and seasonality patterns; however, hypothesis testing indicated that these variations

were not statistically significant. In the Northern region, the replacement of the SARIMA model with an ARIMA model suggests a possible loss of seasonality, which may be associated with underreporting and reduced sensitivity of the surveillance system during the pandemic period.

In our study, the model generated from the dataset that included whooping cough information up to 2024 was used to perform the predictions. At the time of the analysis, data for 2025 were not yet available in DataSUS; therefore, a prediction was generated for that year, estimating 3338 whooping cough cases in 2025. In the latest update (14 November 2025), DataSUS reported 2403 confirmed cases.²⁹ Although this number is lower than our prediction, it remains consistent with the global upward trend, considering that several weeks still remain before the end of the year. Our projections for 2026 indicate an expected increase in cases between May and October in the Southeast region, with similar seasonal patterns predicted from July to December in 2027. Additionally, in the South region, a trend toward higher whooping cough incidence is observed between January and March 2026, extending from August 2026 to December 2027, suggesting significant seasonal variations.

A potential limitation of this study is the occurrence of underreporting, particularly during exceptional events such as the COVID-19 pandemic. However, the results highlight the usefulness of time series models for forecasting infectious diseases. Furthermore, the projected whooping cough scenario for 2026 and 2027 reinforces its relevance as one of the most challenging infectious diseases for public health in Brazil, providing essential information for resource planning, strengthening immunization campaigns, and enhancing epidemiological surveillance during periods of increased risk.¹¹

CONCLUSION

This study demonstrates that, despite the advances achieved through vaccination, whooping cough continues to exhibit a complex epidemiological dynamic in Brazil, characterized by seasonal fluctuations and regional disparities. The reduction in cases between 2020 and 2023, followed by the increase in 2024, reflects the impacts of the COVID-19 pandemic on surveillance, vaccination coverage, and social mobility. Time series models (ARIMA and SARIMA) proved effective in identifying trends and regional patterns, and the projections for 2026 and 2027 indicate a sustained increase in cases. These findings reinforce the importance of continuous surveillance, targeted vaccination strategies, and strategic public health planning, highlighting whooping cough as a persistent challenge in the country.

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AVAILABILITY OF DATA AND MATERIALS

All raw data are available on SINAN / Tabnet / DataSUS. The methodology applied in this study was previously detailed in the protocol “Algorithm with time series simulation versus auto-adjustment in R for predicting tuberculosis cases in Goiás.”

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

AUTHORS CONTRIBUTION

The authors LRBA and LPA contributed equally to the preparation of this article. LRBA and LPA contributed to the conceptualization, methodology, investigation, and creation of the figures. BRNS, IMMO, ALEM, LORM and LRBA: drafting the original manuscript; LRBA and LPA: editing the figures. LPA: statistical analysis and review and editing of the manuscript. All authors agreed on the final version of the manuscript prior to submission.

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MANAGEMENT OF A DIFFICULT AIRWAY IN A CHILD WITH GOLDENHAR SYNDROME: A CASE REPORT

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ABSTRACT

Goldenhar syndrome (GS) is part of the oculoauriculovertebral spectrum (OAVS) characterized by the classic triad of ocular, auricular, and vertebral abnormalities. A 6-month-old, 8.5 kg patient with GS underwent general anesthesia for removal of a cerebral teratoma. Pre-anesthetic evaluation revealed retrognathia, asymmetrical hard palate, and facial asymmetry. Anesthetic induction was by inhalation with 8% sevoflurane combined with 10 mcg of fentanyl, 30 mg of intravenous propofol, and 1.5 mg of cisatracurium. Three attempts at orotracheal intubation were made, the first two via direct laryngoscopy, without glottic visualization, and the third using a videolaryngoscope. In the literature, few cases of successful airway management in GS using a Magill blade, blind intubation, and laryngeal mask airway have been mentioned. Thus, the objective of this article is to report on the management of a difficult airway in a patient with SG.

Keywords: Goldenhar Syndrome, General anesthesia, Airway management, Brain neoplasms, Balanced Anesthesia.

INTRODUCTION

Fibular Goldenhar syndrome (GS) is part of the oculo-auriculo-vertebral spectrum (OAVS) and is recognized by the presence of the classic triad of ocular, auricular, and vertebral anomalies. It is mainly characterized by preauricular appendages, epibulbar dermoid cysts, and hemifacial microsomia, in addition to cardiac, genital, renal, and pulmonary abnormalities.¹

It has a rare incidence of approximately 1 in 56,000 births, with a higher prevalence in males (3:2)¹. Its origin is multifactorial and includes genetic and environmental factors, with the presence of familial cases possibly explaining the genetic basis of the syndrome.² Its pathophysiology involves abnormal development of the first pharyngeal arches, which develop during the fourth week of gestation.³

Diagnosis is based on clinical data, including medical history, physical examination, and results of complementary tests, and may be established either during pregnancy or after birth. Regarding treatment, it is carried out within each specialty, aiming to provide the most appropriate management based on the literature and the experience of the professionals involved.⁴

In this context, patients with GS, due to the presence of facial malformations in their phenotype, are potentially at risk for a difficult airway. Therefore, this article aims to describe the management of a difficult airway in a patient with GS undergoing general anesthesia.

CASE REPORT

A six-month-old male patient, weighing 8.5 kg, diagnosed with Goldenhar syndrome (GS), underwent general anesthesia for resection of a cerebral teratoma.

During the pre-anesthetic evaluation, the patient presented with retrognathia, posterior displacement of the soft palate, asymmetric hard palate, congenital torticollis, microtia, and facial and mandibular asymmetry. Additionally, he had a recent nasofibrolaryngoscopy showing an incomplete and open midline cleft palate and mild glossoptosis. Following this examination, the patient developed apnea during feeding.

Other complementary tests revealed mild right ventricular dilation and hypertrophy on echocardiography, and a normal cervical spine on radiography.

Cranial magnetic resonance imaging demonstrated an expansive cystic lesion located in the suprasellar cistern, with calcifications measuring approximately $2.4 \times 3.3 \times 2.3$ cm, suggestive of a cerebral teratoma. This lesion caused a compressive mass effect on the pontine base, right cerebral hemisphere, and fourth ventricle.

Anesthetic induction was performed using inhalational sevoflurane (8%), associated with intravenous administration of fentanyl 10 micrograms (mcg) and propofol 30 mg. After induction, the patient tolerated mask ventilation without difficulty. Two attempts at orotracheal intubation (OTI) using direct laryngoscopy (conventional laryngoscope) were performed, without visualization of the glottis, even with external neck pressure and use of a bougie.

A new dose of 30 mg propofol and 1.5 mg cisatracurium was administered, and a third laryngoscopy attempt was performed using a videolaryngoscope and bougie, revealing a Cormack-Lehane grade 3B view, with successful OTI using a cuffed endotracheal tube size 4.5 (Figure 1). Anesthesia was then maintained with sevoflurane 2%, without the need for additional intravenous anesthetics or further neuromuscular blockade. Adjunct medications were also administered, including dipyrone 250 mg, dexamethasone 1.5 mg, and ondansetron 1.5 mg.



Figure 1: Patient from the clinical case under general anesthesia.

During the surgical procedure, the patient remained hemodynamically stable and eupneic, under mechanical ventilation. At the end, the patient was extubated without complications and transferred to the Intensive Care Unit (ICU).

DISCUSSION

Craniofacial abnormalities in Goldenhar syndrome (GS) may result in a difficult airway in up to 40% of cases, mainly due to the combination of micrognathia, limited cervical mobility, and tracheal deviation. This represents a challenge for the anesthesiologist and may require the use of alternative methods for laryngoscopy in order to ensure airway patency.^{5,6}

Clinical airway examination should include the assessment and identification of structural malformations. Therefore, features such as palate and mandibular shape, mouth opening, and range of neck movement should be evaluated.⁶

Regarding complementary evaluation, mandibular and cranio-cervical radiological assessment is recommended prior to scheduled surgical procedures. The presence of mandibular hypoplasia identified on imaging, for example, may be considered an individual predictor of a difficult airway, as studies indicate a significant association between the severity of mandibular hypoplasia and the degree of intubation difficulty.⁷

Obstruction of the upper and lower airways during sleep is common in patients with significant craniofacial anomalies, such as those with GS. This finding is important, as it may predict difficult mask ventilation, which was not observed in the patient described, since he tolerated mask ventilation without difficulty after anesthetic induction.

Anticipation of a difficult airway is of paramount importance in patients with GS. In the literature, only a few cases of successful airway management in GS have been reported using a Magill blade, fiberoptic intubation, blind intubation, and laryngeal mask airway. In such situations, it is preferable to use a videolaryngoscope rather than more traditional techniques from the outset.⁸ Thus, a point of criticism in the management of this case is that the videolaryngoscope was not used as the first attempt, but rather the conventional laryngoscope.

Regarding pharmacological effects, the combination of volatile anesthetics, muscle relaxants, and opioids places patients with GS at high risk of postoperative hypoxic events. Therefore, complete recovery of airway reflexes should be confirmed before extubation, as well as postoperative monitoring in an intensive care unit setting.⁹

CONCLUSION

Patients with Goldenhar syndrome (GS) represent a challenge in airway management and in establishing a definitive airway for general anesthesia. Craniofacial anatomical abnormalities may predispose these individuals to a difficult airway, both for mask ventilation and for orotracheal intubation. In this context, it is essential that the anesthesiologist and the team are well trained, and the use of videolaryngoscopy should be considered from the first attempt.

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GIANT MATURE OVARIAN TERATOMA IN A FIRST-TRIMESTER PREGNANT WOMAN: A CASE REPORT

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ABSTRACT

Introduction: Mature cystic teratoma is the most frequent ovarian neoplasm in reproductive-aged women, posing maternal and fetal risks when diagnosed during pregnancy. **Objectives:** To report the diagnosis and surgical management of a giant ovarian teratoma in a first-trimester pregnant patient. **Methods:** A descriptive case report study of a 17-year-old primigravida with a 30 cm adnexal mass concomitant with a 12-week intrauterine pregnancy. **Results:** Exploratory laparotomy with partial drainage of the contents was performed to enable tumor excision, and histopathology confirmed a mature cystic teratoma associated with a mucinous cystadenoma. Prenatal follow-up revealed a borderline lateral ventricle and progression to intrauterine growth restriction (IUGR) in the third trimester, leading to labor induction at 38 weeks. **Conclusions:** This case reinforces the necessity of timely surgical intervention for voluminous adnexal masses during pregnancy and the importance of rigorous obstetric surveillance to monitor perinatal outcomes potentially associated with early surgical stress.

Keywords: Mucinous cystadenoma, Ovarian neoplasms, Fetal growth retardation, Pregnancy complications, Neoplastic, Teratoma, Prenatal ultrasonography.

INTRODUCTION

Adnexal masses during pregnancy have an estimated incidence of 0.2% to 2%¹. Among them, mature cystic teratoma, also known as a dermoid cyst, is the most frequent ovarian neoplasm in women of reproductive age, representing 20% to 40% of ovarian tumors diagnosed during pregnancy.^{1,2}

Mature cystic teratoma originates from primordial germ cells and contains tissues derived from the three germ layers, ectoderm, mesoderm, and endoderm, resulting in the formation of complex structures such as teeth, hair, sebum, bone, and cartilage.^{3,4} They can reach diameters ranging from millimeters to masses that occupy most of the abdominal cavity; however, the average size observed is 5 to 15 cm⁵.

According to the guidelines of the Federação Brasileira das Associações de Ginecologia e

Obstetrícia⁶, transvaginal ultrasonography is the most effective single examination for the initial evaluation and characterization of adnexal masses, with pregnancy testing being necessary in the complete investigation of adnexal masses in women of reproductive age.

Although most teratomas are benign, their persistence during pregnancy entails risks, such as torsion of the adnexal mass, which may lead to necrosis and tissue loss, cyst rupture, leading to chemical peritonitis, intra-abdominal hemorrhage, and obstruction of the birth canal due to mass effect, known as tumor previa,⁷ Larger masses result from accelerated growth or late diagnosis and may increase the risk of complications.^{5,7}

The clinical management of these masses should consider the surgical and anesthetic risk to the pregnant woman/fetus dyad and the risk of acute complications if left untreated. The standard approach recommends that elective surgical intervention be performed in the second trimester of pregnancy, when the risk of miscarriage is lower and organogenesis is complete.^{8,9} However, large-volume masses may imply greater urgency for their removal to allow the pregnancy to progress normally.

In this regard, the present study reports the surgical management of a giant ovarian mature cystic teratoma in a 12-week pregnant woman and the subsequent pregnancy outcome.

CASE REPORT

A 17-year-old female patient sought medical care in September 2024 to begin the investigation of a pelvic mass. During transvaginal ultrasonography (TVUS) performed on 09/16/2024, a large right ovarian cystic image occupying the pelvic cavity, measuring 22 x 10.65 x 16 cm, was identified, accompanied by a heterogeneous solid image measuring 7.8 x 4.04 x 7.53 cm, suggestive of teratoma.

Laboratory tests requested on 10/29/2024 revealed hemoglobin of 14.8 g/dL, hematocrit of 44%, leukocytes of 7,560/mm³, and platelets of 124,000/mm³. Tumor markers were within normal limits, with CA 125 of 8.7 U/mL and CEA of 1.0 ng/mL, and the coagulation profile showed no abnormalities. A non-contrast computed tomography (CT) scan of the abdomen (10/30/2024) confirmed the multiloculated lesion, extending into the mesogastric region, measuring 20.6 x 17.7 x 9.7 cm, with an estimated weight of 1,839 g.

On 12/12/2024, the patient underwent a new ultrasound examination that diagnosed an intrauterine pregnancy of 11 weeks and 2 days, with the presence of a posterior marginal placenta previa and persistence of the solid-cystic adnexal image (Figure 1). The patient was admitted on 12/18/2024 for surgical planning, clinically asymptomatic, with fetal heart rate (FHR) of 148 BPM and a gestational age of 12 weeks and 1 day.



Figure 1: Ultrasound images of the solid-cystic adnexal structure (A and 1B) and the gravid uterus (2B).
Source: the authors.

The surgical approach was performed on 12/20/2024 by exploratory laparotomy under spinal anesthesia. Examination of the cavity revealed a right ovarian mass measuring approximately 30 cm, with a cystic-solid appearance, reaching the costal margin. Peritoneal fluid was collected for cytology, and due to the exceptional dimensions of the lesion, two small incisions in the mass were necessary for drainage and evacuation of the liquid content, allowing reduction of the tumor volume to enable its removal through the laparotomy opening, via the Pfannenstiel incision (Figure 2). The aspirated content revealed greenish fluid and the presence of hair and teeth. Right salpingo-oophorectomy was performed, and the material was sent for anatomopathological examination, which confirmed the diagnosis of mature cystic teratoma, showing tissues of ectoderm, mesoderm, and endoderm, associated with mucinous cystadenoma.

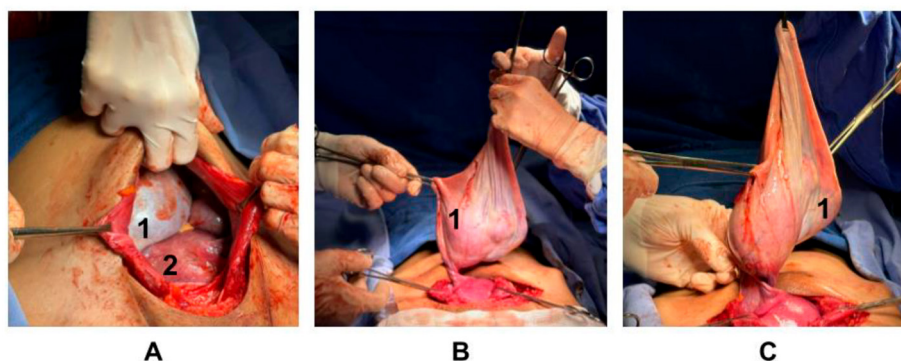


Figure 2: Surgical approach by exploratory laparotomy for resection of the mature cystic teratoma. In 1, the mature cystic teratoma is shown, and in 2, the gravid uterus.

Source: the authors.

The patient had a good postoperative course and continued prenatal follow-up at the service. On 03/12/2025, the morphological ultrasound (24 weeks and 1 day) identified a male fetus with weight at the 9th percentile and a borderline right lateral ventricle (10 mm). In the third trimester, on 05/07/2025 (32 weeks and 1 day), the fetus was observed to be small for gestational age (7th percentile), although with normal Doppler findings. On 06/18/2025, at 38 weeks and 1 day, ultrasonography diagnosed Intrauterine Growth Restriction (IUGR), with fetal weight below the 3rd percentile (2,432 g). In view of the diagnosis of IUGR and the report of epigastric pain and contractions, the patient was admitted for induction of labor on 06/18/2025 at 38 weeks and 1 day.

DISCUSSION

Mature cystic teratoma is the most frequent ovarian tumor in women of reproductive age, representing approximately 50% of tumors diagnosed in women up to 40 years of age.^{2,5,7,10} In the reported case, the 17-year-old patient reinforces this epidemiology.

Imaging diagnosis of this tumor in the patient occurred before the date of the last normal menstrual period (LMP); however, after confirmation by magnetic resonance imaging and during the preparatory examination for the surgical approach, pregnancy was diagnosed. Thus, the tumor became a gestational

complication, while the pregnancy posed a dilemma regarding its surgical resection and created the need for its follow-up concomitantly with the pregnancy-puerperal cycle.

In the present case, although the tumor dimensions greatly exceeded the usual ultrasound criteria for low risk (<10 cm), the patient's young age (17 years), the absence of previous persistent symptoms, and normal CA 125 levels supported the preoperative hypothesis of a benign etiology. However, in accordance with the recommendations of the RBGO⁶, it should be emphasized that the use of isolated biomarker panels is not sufficient for the definitive characterization of the lesion, requiring close ultrasound correlation. Thus, the diagnostic imaging investigation protocol and surgical planning adopted in the present case are in accordance with the recommendations of the RBGO.

The literature recommends that ovarian masses larger than 6 cm be removed so that the pregnancy can proceed without the complications frequently associated with this tumor, such as torsion of the adnexal mass, tumor rupture with consequent chemical peritonitis, and obstruction of the birth canal by tumor previa.^{11,12,13} Large masses extending beyond the pelvis require combined transabdominal and transvaginal ultrasound evaluation.⁶

In the presence of a 30-cm solid-cystic lesion reaching the costal margin, classic exploratory laparotomy proved to be the safest approach to ensure adequate hemostatic control and uterine integrity, allowing a definitive surgical approach, rather than the laparoscopic approach, a technique that is more recommended for tumors smaller than 10 cm.^{3,13}

The ideal period recommended for intervention is the second trimester of pregnancy, preferably between the 16th and 20th weeks, aiming to minimize the risks of miscarriage.^{9,11,12} However, the approach at the end of the first trimester in the reported case did not represent a prohibitive surgical complication, since organogenesis, the critical period of fetal development, had already been completed. However, it removed the mass that occupied the space necessary for the fetus to grow during the subsequent stages of pregnancy.

The preserved fetal morphology in the morphological examinations subsequent to the intervention corroborates the evidence that modern anesthetic agents, muscle relaxants, and opioids have no proven teratogenic effects on the development of human fetuses when administered at recommended doses, regardless of gestational age.^{9,12} However, non-obstetric surgical interventions during pregnancy are associated with a statistically significant increase in the risks of obstetric complications and adverse perinatal outcomes.^{6,9}

The diagnosis of Intrauterine Growth Restriction (IUGR) and the classification of the fetus as Small for Gestational Age (EFW < P3), identified in the patient's third trimester, may reflect the acute ischemic stress and systemic inflammatory response generated by early surgery, since such interventions are statistically associated with a greater likelihood of growth restriction and low birth weight.^{3,9,14}

Furthermore, the finding of a borderline right lateral ventricle at 24 weeks, although it may be an isolated variant, reinforces the need for strict surveillance, since surgeries in the first and third trimesters have the highest rates of obstetric complications, including the need for pregnancy termination due to premature contractility, as observed in the outcome of this case.^{9,12}

CONCLUSION

The surgical approach to the giant ovarian mature cystic teratoma, diagnosed during the preconception period in the reported case, became essential and urgent due to the size and inherent risks of this mass. The pregnancy diagnosed during clinical follow-up became a complicating factor and posed a challenge to the removal of the tumor mass, since in cases of tumors during pregnancy,

care for the maternal-fetal dyad must be considered.

Therefore, this case demonstrates the importance of early diagnosis of mature cystic teratoma in order to prevent such extensive tumor growth. However, in the case of this tumor concomitant with pregnancy, the need for timely and appropriate surgical removal is evident, in addition to rigorous multidisciplinary prenatal follow-up to mitigate adverse obstetric outcomes.

Ethical Aspects

The study was approved by the institution's Research Ethics Committee under CAAE number: 96379426.1.3001.5078. Written informed consent was obtained from the patient and her legal guardians for the publication of this case report and the accompanying images.

The Artificial Intelligence (AI) tools Gemini Notebook were used for textual correction and translations and Scispace for searching for scientific articles related to the topic.

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FIBULAR TIBIALIZATION FOR THE RECONSTRUCTION OF SEGMENTAL TIBIAL DEFECTS

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ABSTRACT

Introduction: Fibular tibialization, initially proposed by Hahn and later refined by Huntington, is a reconstructive technique used to manage extensive tibial segmental defects. It represents a biological autologous alternative, particularly valuable when conventional methods such as isolated bone transport or large grafting are not feasible. Gustilo-Anderson IIIC open tibial fractures remain among the most challenging orthopedic injuries, often requiring complex multidisciplinary limb salvage strategies. **Objective:** To report and analyze the first case of fibular tibialization performed at the Hospital Estadual de Anápolis Dr. Henrique Santillo (HEANA), emphasizing its applicability for limb salvage following high-energy trauma with extensive bone loss. **Case Report:** A patient involved in a motorcycle accident sustained a severe Gustilo-Anderson IIIC open fracture of the left tibia, associated with vascular injury and a 12 cm segmental bone defect. Initial management included temporary external fixation, fasciotomy, revascularization, and serial debridements. After adequate soft tissue coverage, fibular osteotomy and gradual medial transport were performed using an Ilizarov circular external fixator. The course required multiple surgical revisions, complementary tibial bone transport, autologous tricortical iliac crest grafting, and progressive consolidation. Late sequela included rigid equinus deformity, treated with ankle arthrodesis. **Conclusion:** Fibular tibialization combined with the Ilizarov technique is an effective limb salvage option for severe open tibial fractures with extensive segmental bone loss. This case highlights the importance of staged multidisciplinary management and demonstrates the feasibility of advanced reconstructive approaches in the Brazilian hospital setting.

Keywords: Tibia, Open fractures, Fibular tibialization, Ilizarov external fixator, Limb salvage, Segmental bone defect.

INTRODUCTION

Fibular tibialization, also known as the “fibula pro tibia” technique, was initially proposed by Hahn in 1884 as an alternative to fill extensive tibial defects through transposition of the ipsilateral fibula. Later, Huntington, in 1903, successfully applied this approach in a seven-year-old boy with a 12.7 cm tibial defect, using a pedicled vascularized graft in two stages, with establishment of proximal synostosis and observation of progressive graft hypertrophy after gradual weight-bearing.¹

The modern evolution of the technique especially emphasizes its use in children, with preservation

of the distal fibular growth plate. Baptista and collaborators highlight that autotransplantation of the distal fibular physis allows limb equalization during growth, being performed through a single approach and modification in the bone transposition route. This approach uses an arc-shaped incision that simultaneously reaches the tibial and fibular regions, allowing almost complete transposition of the fibula as an autologous biological solution, without the need for microsurgery.²

The procedure involves transfer of the fibula associated with the peroneal muscles and the tibialis anterior muscle, supported by a vascular pedicle from the peroneal vessels. This biological component of living bone favors a shorter consolidation time, greater remodeling capacity, superior resistance to infection, and better long-term mechanical properties.^{1,3}

The main indications for fibular tibialization include extensive tibial bone loss greater than 6 cm, failure of conventional reconstruction methods, adequate limb vascularization, preserved plantar sensation, and integrity of the ipsilateral fibula, even in cases of fracture that can still be used. In contrast, absolute contraindications include severe vascular compromise, uncontrolled active infection, loss of plantar sensation, and limited life expectancy.⁴

Several authors report that tibialization constitutes a viable option for limb salvage in cases of extensive tibial defects and complex healing. Tuli describes the technique as an effective alternative in difficult reconstructions, while Wood, in his 25-year experience with free vascularized fibular grafts, highlights satisfactory results when well indicated. However, complications such as nonunion, infection, angular deformities, limb shortening, and joint functional limitation are described in the literature as possible adverse outcomes.^{5,6}

Although bone transport using the Ilizarov technique is often considered the procedure of choice for extensive tibial defects, there are situations in which the tibial remnant is inadequate for lengthening, requiring alternative approaches. Catagni et al. described medial transport of the fibula with an Ilizarov fixator as an effective alternative in massive tibial bone loss. Intramedullary fixation has been considered biomechanically superior, allowing consolidation of the tibiofibular junctions and progressive hypertrophy within a few months, reaching dimensions comparable to the original tibia within up to three years.⁷

The present project aims to document and analyze a case of fibular tibialization performed at the Hospital Estadual de Anápolis Dr. Henrique Santillo (HEANA), this being the first procedure of this nature performed at the institution. Its relevance is related not only to the complexity of the technique, but also to the need to evaluate its applicability and effectiveness in the Brazilian hospital context. Thus, this study will contribute to the national literature in reconstructive orthopedics, offering clinical data and serving as a reference for professionals facing similar challenges.

Despite the generally favorable results described, in extremely severe cases it may be preferable to opt for immediate amputation, avoiding prolonged, painful treatments with risk of repeated failure that may eventually culminate in late amputation. Therefore, appropriate patient selection and a clear understanding of the indications and contraindications are fundamental to therapeutic success.

CASE REPORT

The patient was admitted on 08/06/2022 to HEANA, victim of a motor vehicle accident (motorcycle versus car collision), presenting with an extremely severe open fracture of the left tibia (Gustilo-Anderson IIIC), associated with extensive soft tissue loss and loss of distal perfusion.

Table 1 : Chronology of the Patient's Care.

Date	Stage / Surgery	Procedure Performed	Objective / Observations
08/06/2022	Initial care (emergency)	Temporary external fixation + fasciotomy + revascularization (popliteal artery injury)	Damage control, limb salvage, and restoration of distal perfusion
08/06/2022	Follow-up surgery	Debridement + fasciotomy revision	Removal of devitalized tissues and initial contamination control
08/06/2022	Follow-up surgery	Debridement + resection of necrotic bone	Infection control and preparation of the bone bed
09/02/2022	Follow-up surgery	Debridement + Figueiredo-type dressing	Wound management and assistance in infection control
09/06/2022	Hospital discharge	—	After 30 days of hospitalization and multiple initial interventions
10/07/2022	Outpatient follow-up	Beginning of outpatient bone reconstruction follow-up	Initial identification of the bone defect
11/03/2022	Reconstructive evaluation	Tibial defect of approximately 12 cm	Therapeutic discussion: amputation vs. fibular tibialization
12/26/2022	Soft tissue reconstruction	Debridement + skin graft + flap on the left leg	Adequate coverage and preparation of the recipient bed
02/22/2023	Surgery 1	Fibular osteotomy + fixation with dynamic circular fixator (Ilizarov)	Beginning of the progressive transposition of the fibula to the tibia
03/01/2023	Surgery 2	Repositioning of the fixator + replacement of Schanz pins	Correction due to loosening of pins and continuation of transport
30/05/2023	Surgery 3	Complete transposition of the fibula + distal telescoping + distal osteotomy	Insertion into the distal tibial canal to promote consolidation

Date	Stage / Surgery	Procedure Performed	Objective / Observations
02/11/2023	Surgery 4	Revision due to hardware failure + replacement of metaphyseal pins + distal tibial osteotomy + new assembly	Proximal tibial bone transport to cover the residual defect
04/03/2024	Surgery 5	Enxerto ósseo tricortical autólogo da crista ilíaca	Proximal tibial bone transport to cover the residual defect
09/25/2024	Radiographic evaluation	Consolidação proximal e distal + consolidação do regenerado tibial	Evidence of satisfactory bone union
11/06/2024	Fixator removal	Removal of the circular fixator + joint manipulation	Gain in mobility and functional progression
12/11/2024	Rehabilitation	Progression to full weight-bearing + intensive physiotherapy	Motor recovery and biomechanical adaptation
25/02/2025	Surgery 6	Ankle arthrodesis + plantar flexor tenotomy	Correction of late sequela: rigid equinus foot
12/11/2025	Outpatient discharge	Complete consolidation + gait with residual claudication	Reduced muscle strength and functional limitation compatible with the initial severity

Cirurgia	Data	Procedimento Realizado
Cirurgia 1	22/02/2023	Transposição da fibula para tibia com fixador circular dinâmico.
Cirurgia 2	01/03/2023	Reposicionamento de fixador com troca de pinos de Schanz.
Cirurgia 3	30/05/2023	Transposição completa da fibula e osteotomia distal.
Cirurgia 4	02/11/2023	Revisão por falha de material e transporte ósseo proximal.
Cirurgia 5	03/04/2024	Enxertia óssea tricortical da crista ilíaca.
Cirurgia 6	25/02/2025	Artrodese de tornozelo e correção do pé equino.

Figure 1 : Data on surgeries and procedures performed.

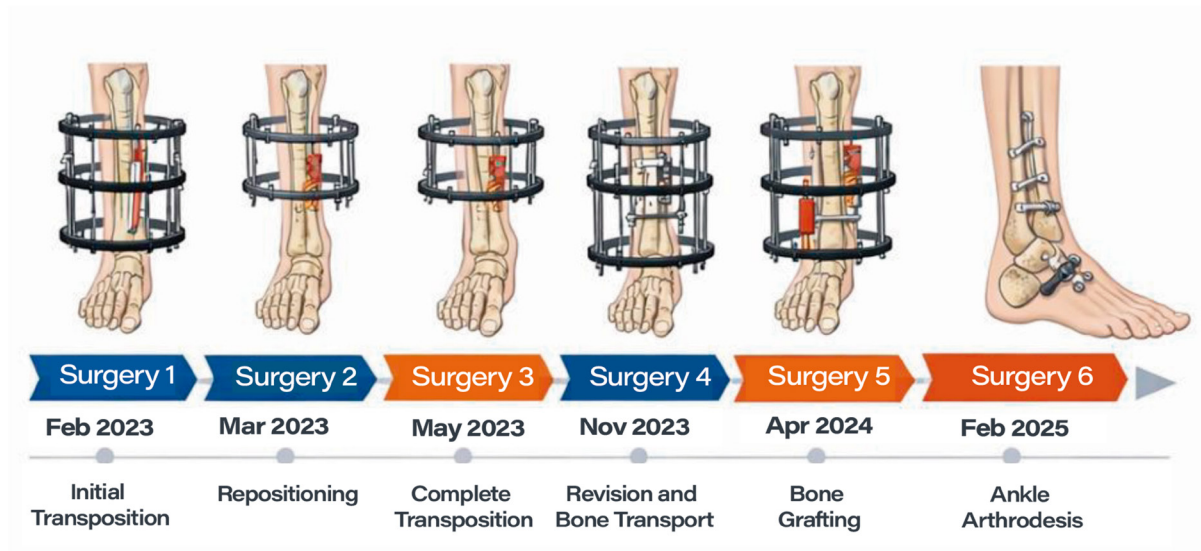


Figure 2: Models of the surgeries performed.

DISCUSSION

The presented case illustrates the complex reconstruction of a lower limb following high-energy trauma, culminating in a Gustilo-Anderson IIIC open fracture of the tibia with a 12 cm segmental bone defect. The decision to perform fibular tibialization, associated with bone transport using a circular Ilizarov fixator, represents a robust limb salvage strategy and is aligned with the scientific literature for cases of extreme severity.^{8,9}

The Gustilo-Anderson IIIC classification, characterized by arterial injury requiring repair for

limb viability, represents the extreme end of the spectrum of open fractures, with historically high amputation rates.¹⁰ A recent systematic study demonstrated that, although the decision between limb salvage and primary amputation remains controversial, functional outcomes and quality of life may be comparable between the two groups, reinforcing the validity of attempting reconstruction in selected patients.¹¹ The initial approach in this case, involving damage control, serial debridements, fasciotomy, and revascularization, followed the fundamental principles of severe trauma management, aiming at patient stabilization and the creation of a viable bed for subsequent reconstruction.¹²

The choice of fibular tibialization, or the Huntington procedure, was particularly appropriate given the extent of the bone defect. This technique, although described more than a century ago, remains a valuable alternative, especially when other options such as monofocal bone transport or free vascularized fibular grafting are unfeasible or present high risks.¹³ The main advantage of tibialization is the use of the ipsilateral fibula as a pedicled vascularized bone graft, which, once transposed to the tibial position and subjected to load, undergoes a process of adaptive hypertrophy, becoming capable of supporting body weight. Studies demonstrate that the tibialized fibula may reach diameters comparable to those of the contralateral tibia, a process that is more pronounced in younger patients, but which also occurs effectively in adults.¹⁴

The use of the circular Ilizarov fixator was crucial at multiple stages of treatment. Initially, it allowed the gradual transposition of the fibula, and later it was adapted to perform bone transport of the proximal tibial segment, addressing the residual defect. The Ilizarov technique, based on the principle of distraction osteogenesis, is considered the gold standard for the treatment of large bone defects, allowing regeneration of autologous bone and the simultaneous treatment of deformities and length discrepancies.¹⁵ The combination of tibialization with bone transport, as performed in this case, is a powerful hybrid approach that optimizes reconstruction by biologically filling large bone defects.

The long treatment time, extending for more than two years and involving multiple surgical interventions, is an inherent characteristic of these complex reconstruction processes. Complications such as pin loosening and hardware failure are relatively common and are part of the learning curve and the challenges associated with the prolonged use of external fixators.¹⁶ The proactive management of these complications, with planned surgical revisions, was fundamental to the final success of the treatment.

The sequela of rigid equinus foot, which required ankle arthrodesis, is a known complication and is frequently associated with severe lower limb trauma, neurological injuries, and long periods of immobilization with an external fixator. Arthrodesis, by creating a fused and stable joint, provides a plantigrade platform for gait, improving function and relieving pain, although at the expense of ankle mobility.¹⁷

CONCLUSION

The final outcome, with the patient ambulating under full weight-bearing despite residual functional limitations, should be considered a success. The literature supports that, for Gustilo IIIC fractures, the primary objective is the achievement of a functional and pain-free limb, and not necessarily the complete restoration of pre-injury function. The case demonstrates the effectiveness of a multidisciplinary and staged approach, combining plastic surgery techniques for soft tissue coverage and advanced

reconstructive orthopedic surgery for the treatment of the bone defect, resulting in limb preservation in a scenario with an extremely high risk of amputation.

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INTRAUTERINE BLOOD TRANSFUSION IN SEVERE PERINATAL HEMOLYTIC DISEASE: A CASE REPORT

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ABSTRACT

The objective of this work is to describe and analyze the clinical management of a pregnant woman with perinatal hemolytic disease (PHD) undergoing intrauterine blood transfusion (IUT), with emphasis on the main diagnostic, therapeutic, and prognostic points involved in the case. The specific objectives are: to present the main aspects of perinatal hemolytic disease; to describe the diagnostic processes of the disease; and to analyze intrauterine blood transfusion in patients with perinatal hemolytic disease. The severity of the case is related to the high titer of maternal anti-Rh fetal antibodies (titration: 1/2048) and the number of transfusions, which was far above the usual average (9 transfusions).

Keywords: Anti-d antibodies, Perinatal hemolytic disease, RH factor, Pregnancy, Intrauterine transfusion.

INTRODUCTION

Perinatal hemolytic disease (PHD) is one of the most relevant immunological complications associated with pregnancy, characterized by the destruction of fetal red blood cells mediated by maternal antibodies capable of crossing the placental barrier. It is a potentially severe condition that may result in progressive fetal anemia, heart failure, fetal hydrops, and intrauterine death, especially when not diagnosed or treated in a timely manner.¹

Historically, PHD has been strongly associated with incompatibility of the Rh system, particularly related to the D antigen. Before the introduction of anti-D immunoglobulin prophylaxis, this condition was responsible for high rates of perinatal morbidity and mortality. Despite advances in prevention, the disease persists as a public health problem, particularly in countries with limited access to adequate prenatal care or failures in the implementation of preventive strategies.²

In cases of maternal sensitization, the IgG antibodies produced recognize fetal erythrocyte antigens as foreign, triggering a process of chronic hemolysis. This erythrocyte destruction compromises fetal oxygenation, leading to cardiovascular adaptations that, when exceeding the fetus's compensatory capacity, result in severe conditions such as fetal hydrops.³

In this context, intrauterine blood transfusion (IUT) has been established as one of the most important

therapeutic interventions in the management of severe fetal anemia secondary to PHD. The procedure consists of the direct infusion of packed red blood cells into the fetal circulation, allowing rapid correction of anemia, improvement of tissue oxygenation, and significant reduction in intrauterine mortality rates.⁴

The main objective of this study is to describe and analyze the clinical management of a pregnant woman with perinatal hemolytic disease (PHD) who underwent intrauterine blood transfusion (IUT), with emphasis on the main diagnostic, therapeutic, and prognostic aspects involved in the case. The specific objectives are: to present the main aspects of perinatal hemolytic disease; to describe the diagnostic processes of the disease; and to analyze intrauterine blood transfusion in patients with perinatal hemolytic disease.

Severity was based on the anti-Rh antibody titer (1:2048) and the high number of transfusions.

LITERATURE REVIEW

Perinatal Hemolytic Disease

Perinatal hemolytic disease (PHD) is defined as an immunological condition resulting from incompatibility between antigens present on fetal red blood cells and specific maternal antibodies, leading to the destruction of these blood cells either during intrauterine life or in the early neonatal period. This incompatibility occurs predominantly when the mother is previously sensitized to erythrocyte antigens inherited by the fetus from the father.²

The main characteristic of PHD is the progressive hemolysis of fetal red blood cells mediated by IgG immunoglobulins, which are capable of crossing the placenta. The severity of the disease varies according to the type and titer of maternal antibodies, as well as the fetus's compensatory capacity, and may range from mild forms to severe cases with systemic involvement.⁵

Clinically, PHD may manifest as fetal anemia, neonatal hyperbilirubinemia, jaundice, hepatosplenomegaly, and, in more severe cases, fetal hydrops. The severity of the condition is directly related to the rate of erythrocyte destruction and gestational maturity, with early diagnosis being a determining factor for therapeutic success.⁶

Rh incompatibility, particularly related to the D antigen, is considered the main classical cause of perinatal hemolytic disease. This condition occurs when an Rh-negative pregnant woman is exposed to Rh-positive fetal red blood cells, usually during delivery, miscarriage, invasive procedures, or episodes of transplacental bleeding, leading to maternal immunological sensitization.¹

After sensitization, the mother begins to produce anti-D antibodies which, in subsequent pregnancies with Rh-positive fetuses, cross the placenta and promote the destruction of fetal red blood cells. The intensity of the immune response may increase progressively with each exposure, raising the risk of severe forms of the disease.⁷

Despite the widespread use of anti-D immunoglobulin prophylaxis having significantly reduced the incidence of PHD due to Rh incompatibility, this etiology is still observed in contexts of prophylaxis failure, late diagnosis, or lack of adequate prenatal care.⁵

Diagnosis of Hemolytic Disease

Maternal diagnosis of perinatal hemolytic disease is an essential step in the prevention, early identification, and appropriate management of the condition. Systematic evaluation during prenatal care allows the identification of pregnant women at risk of alloimmunization and the implementation of timely preventive or therapeutic measures.¹

Early identification of maternal blood group and Rh factor is considered one of the main strategies for preventing perinatal hemolytic disease. Blood typing should preferably be performed at the first prenatal visit, enabling the identification of Rh-negative pregnant women at potential risk of sensitization.⁶

In Rh-negative pregnant women, determination of the paternal Rh factor and careful monitoring throughout pregnancy are fundamental for the prevention of alloimmunization. Prophylactic administration of anti-D immunoglobulin, when indicated, has significantly reduced the incidence of perinatal hemolytic disease associated with the Rh system.⁷

Despite advances in prophylaxis, failure to identify the Rh factor early or lack of adequate follow-up remain factors associated with the occurrence of severe cases of the disease, particularly in settings with inadequate prenatal care.

Screening for irregular antibodies, performed using the indirect Coombs test, is essential for detecting maternal antibodies capable of causing fetal hemolysis. This test allows not only the identification of antibodies but also their titration, assisting in the assessment of fetal risk.²

Serial antibody titration is used to monitor the progression of alloimmunization throughout pregnancy. High or rising titers are associated with a greater risk of severe fetal anemia, although the correlation between titer and severity is not absolute, especially in cases involving antibodies of the Kell system. Pregnant women with a history of moderate or severe perinatal hemolytic disease and initial anti-D antibody titers equal to or greater than 1:128 have a 3.3-fold higher risk of requiring intrauterine transfusion or progressing to fetal death during prenatal follow-up. On the other hand, the presence of anti-D antibodies associated with other anti-erythrocyte antibodies did not show a significant relationship with the evaluated outcomes.⁷

Early detection of irregular antibodies allows referral of the pregnant woman to specialized fetal medicine centers, where appropriate follow-up can be performed and therapeutic interventions instituted when necessary.⁶

Obstetric ultrasonography is a fundamental tool in fetal evaluation, allowing the identification of indirect signs of anemia. Among the most relevant findings are cardiomegaly, hepatosplenomegaly, and the presence of fetal hydrops, which indicate hemodynamic decompensation. Hepatosplenomegaly reflects increased extramedullary erythropoiesis, while cardiomegaly indicates cardiac overload secondary to anemia. The identification of these ultrasonographic findings reinforces the need for detailed investigation and close monitoring.⁶ The presence of fetal hydrops is a marker of severity and is associated with a worse prognosis, requiring immediate intervention to reduce the risk of intrauterine death.

Doppler ultrasound of the middle cerebral artery (MCA) is considered the main noninvasive method for screening fetal anemia, especially in high-risk pregnancies, such as those involving Rh alloimmunization. This examination evaluates the peak systolic velocity of blood flow in the MCA, which is increased in anemic fetuses due to reduced blood viscosity. Peak systolic velocity values greater than 1.5 multiples of the median (MoM) are associated with a high probability of moderate to severe fetal anemia. The use of this method has the significant advantage of reducing the need for invasive procedures, such as cordocentesis, in approximately 50% to 70% of cases, thereby decreasing fetal risks. MCA Doppler is generally performed every one to two weeks, starting from the 16th to 18th week of gestation.⁶

Intrauterine Blood Transfusion

Intrauterine blood transfusion (IUT) is defined as an invasive fetal medicine procedure that consists of the infusion of packed red blood cells directly into the fetal circulation, with the main objective of

correcting severe fetal anemia. This intervention aims to restore oxygen-carrying capacity, reduce tissue hypoxemia, and prevent progression to heart failure and fetal hydrops.⁸

In the context of perinatal hemolytic disease, IUT represents the main therapeutic modality capable of interrupting the cycle of progressive hemolysis. By increasing fetal hemoglobin levels, the procedure promotes immediate improvement in systemic oxygenation and hemodynamic stabilization, allowing the continuation of pregnancy to safer gestational ages for delivery.⁹

The procedure is performed under strict ultrasound guidance, ensuring continuous visualization of fetal structures and the puncture site. The most commonly used approach today is the intravascular route, with access to the umbilical vein, considered the safest and most effective technique. This approach allows rapid correction of anemia and direct monitoring of the fetal response to treatment.³

IUT is primarily indicated in cases of moderate to severe fetal anemia, diagnosed by noninvasive or invasive methods, and should be performed in specialized centers with a multidisciplinary team experienced in invasive fetal medicine. Despite its invasive nature, when properly indicated and performed, it has a high success rate and a positive impact on perinatal outcomes.⁴

The historical evolution of intrauterine blood transfusion reflects technological and scientific advances in fetal medicine. The first attempts to treat fetal anemia occurred in the 1960s, when transfusion was performed via the intraperitoneal route, a pioneering technique that consisted of infusing blood into the fetal abdomen, allowing gradual absorption through the lymphatic system.⁹

Although innovative for its time, the intraperitoneal approach had significant limitations, such as unpredictable absorption of the transfused volume, delayed therapeutic response, and a higher risk of failure in cases of fetal hydrops. These limitations led to the development of more precise and effective techniques, culminating in the introduction of intravascular intrauterine transfusion.³

With improvements in real-time ultrasonography and Doppler velocimetry, direct access to the fetal circulation became possible, particularly to the umbilical vein near the placental insertion. This approach enabled greater procedural control, immediate correction of anemia, and a significant reduction in complications associated with the technique.⁴

Currently, intravascular intrauterine blood transfusion is considered the gold standard for the treatment of severe fetal anemia. Technical advancements have played a decisive role in reducing fetal mortality associated with perinatal hemolytic disease, transforming the management of this condition and expanding the possibilities for survival and favorable neonatal outcomes.

CASE REPORT

Patient D.A., 31 years old, blood type O negative, G3P3N1C2A0. The first child was born with blood type O positive, and the second A positive. All children are from the same partner, who is A positive. At the beginning of the third pregnancy, the patient presented with transvaginal bleeding, and ultrasound identified a small placental abruption, for which Utrogestan 200 mg and relative rest were prescribed.

She had not received human immunoglobulin in previous pregnancies; however, the indirect Coombs test (ICT) was negative at that time. At 20 weeks of gestation, the patient presented an ICT titer of 1:2048. A morphological ultrasound was performed at 22 weeks, and Doppler of the middle cerebral artery (MCA) was abnormal, indicating a positive screening for fetal anemia. Subsequently, a diagnostic cordocentesis was performed, identifying fetal blood group O positive, positive direct Coombs test, and fetal anemia based on hematocrit and hemoglobin levels. At 24 weeks, intrauterine blood transfusions

were initiated under ultrasound guidance and local anesthesia, totaling nine transfusions, performed via the intraperitoneal route, with volumes ranging from 70 mL to 95 mL of O-negative blood.

At 25 weeks of gestation, another cordocentesis was performed with the collection of 3 mL of fetal blood, without complications. Fetal blood typing at this evaluation confirmed O positive. Fetal Doppler ultrasound performed at 28 weeks showed no abnormalities. Additional Doppler ultrasounds were performed, all demonstrating normal flow, normal hemodynamic profile, and normal myocardial function.



Figure 1: Obstetric ultrasound with Doppler at 23 weeks.

The patient received corticosteroid therapy for fetal lung maturation, and a cesarean section was performed at 34 weeks and 6 days of gestation. The newborn was delivered weighing 2070 g, with an Apgar score of 8/9. Umbilical cord blood analysis showed a negative direct Coombs test and blood type O negative, a result likely influenced by the intrauterine transfusions.

The newborn was admitted to the Intensive Care Unit (ICU) due to respiratory distress. On physical examination, the infant presented with a distended abdomen, soft and non-tender on palpation, liver palpable 2.0 cm below the costal margin, palpable splenic tip, and present bowel sounds. There was no evidence of hydrops or edema. Single and double phototherapy were initiated. Laboratory findings showed: red blood cells $6.4 \times 10^{12}/L$, hemoglobin 19.0 g/dL, hematocrit 51.1%, total leukocytes 5,730/ μL , total bilirubin 10.60 mg/dL, direct bilirubin 0.71 mg/dL, and indirect bilirubin 9.89 mg/dL. The newborn evolved with elevated hemoglobin and moderate indirect hyperbilirubinemia, without indications for exchange transfusion or human immunoglobulin therapy. Transfontanelle ultrasound was normal, as was the upper abdominal ultrasound. The fetal echocardiogram revealed a small ostium secundum atrial septal defect (ASD) measuring 3.5 mm. After 10 days, repeat laboratory tests demonstrated favorable clinical evolution: hemoglobin 15.1 g/dL, hematocrit 42.4%, total bilirubin 3.50 mg/dL, direct bilirubin 0.66 mg/dL, and indirect bilirubin 2.84 mg/dL. The newborn was discharged nineteen days later in good general condition.



Figure 2: Newborn in the incubator.

DISCUSSION

Perinatal hemolytic disease (PHD) remains a highly relevant condition in obstetric practice, even with the consolidation of anti-D immunoprophylaxis. The introduction of anti-Rh immunoglobulin in the 1960s marked a significant turning point in the control of maternal isoimmunization, substantially reducing the occurrence of the most severe forms of the disease (Nardoza, 2020). Studies indicate that, when correctly administered in the postpartum period and in risk situations such as miscarriages and invasive procedures, prophylaxis can reduce maternal sensitization by up to 85–90% of cases.⁷

In the case described, the absence of immunoprophylaxis in previous pregnancies was the main factor leading to the development of maternal alloimmunization. The patient reached the 20th week of gestation with an indirect Coombs titer of 1:2048, an extremely high value directly associated with a high risk of severe fetal anemia.

Dantas et al.⁷ report that titers equal to or greater than 1:128 are associated with a substantially increased risk of requiring intrauterine transfusion or resulting in fetal death. Therefore, the patient's clinical condition required intensive follow-up in a specialized referral center.

Doppler velocimetry of the middle cerebral artery (MCA) has been established as a valuable noninvasive tool for screening fetal anemia in the context of PHD. When peak systolic velocity exceeds 1.5 multiples of the median (MoM), there is high sensitivity for detecting moderate to severe anemia, allowing unnecessary invasive procedures to be avoided.⁶ In the present case, serial Doppler assessments demonstrated maintenance of the fetal hemodynamic profile after each transfusion, confirming a satisfactory therapeutic response and clinical stability.

Intrauterine blood transfusion (IUT) is recognized as the gold standard treatment for severe fetal anemia associated with Rh alloimmunization.⁸ The procedure promotes immediate recovery of fetal hemoglobin levels, improvement in oxygenation, and prevention of progression to hydrops. Arnold et al.⁴ emphasize that, when performed by a trained team in a specialized center, IUT has a high success rate and a direct impact on perinatal survival.

In this report, nine intrauterine transfusions were performed via the intraperitoneal route. Although

the intravascular route is currently the preferred approach in most centers, the intraperitoneal technique remains a clinically appropriate alternative in specific scenarios, particularly when fetal vascular access is unfavorable.³ The absence of fetal hydrops and the preservation of myocardial function throughout follow-up demonstrate the effectiveness of the treatment and the progressive control of anemia.

Delivery occurred at 34 weeks and 6 days, preceded by corticosteroid therapy for fetal lung maturation—a measure widely recommended to reduce respiratory morbidity in preterm neonates.⁹ The newborn presented with elevated hemoglobin levels and moderate indirect hyperbilirubinemia, without indication for exchange transfusion.

The negative direct Coombs test and identification of blood type O negative in the neonate are likely attributable to the cumulative effect of intrauterine transfusions, with partial replacement of the fetal erythrocyte pool by donor red blood cells, a phenomenon widely documented in the literature.⁴

The favorable neonatal outcome reinforces the central importance of early diagnosis, continuous monitoring, and timely intervention in the management of PHD. Cunha et al.⁵ highlight that the integrated work of obstetricians, hematologists, neonatologists, and nursing staff is crucial for achieving better perinatal outcomes.

However, despite notable technical and scientific advances, significant structural challenges persist in Brazil, particularly regarding equitable access to anti-D immunoglobulin and the quality of prenatal care across different regions. National scientific literature demonstrates that gaps in prevention still account for a substantial proportion of severe PHD cases.²

CONCLUSION

The present study reinforces the data available in the literature by demonstrating that intrauterine transfusion, when indicated based on appropriate clinical criteria and performed in an adequate setting, is a safe and effective procedure capable of significantly improving fetal prognosis. The case also highlights the urgency of strengthening preventive policies, expanding access to immunoprophylaxis, and investing in the continuous training of healthcare teams in order to reduce the incidence and severity of perinatal hemolytic disease throughout the country.

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COMBINED PERCUTANEOUS TREATMENT OF GIANT ARTERIOVENOUS MALFORMATION AND COMPLEX CORONARY LESIONS IN A HIGH-RISK SURGICAL PATIENT: A CASE REPORT

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ABSTRACT

Coronary artery fistulas (CAF) are considered rare congenital anomalies, characterized by direct communications between the coronary arteries and cardiac chambers or great vessels. Their prevalence is estimated at 0.2% to 0.4% of congenital heart defects. Their etiology is related to abnormalities in embryonic development. The right coronary artery (RCA) and the left anterior descending artery (LAD) are the most common sites of origin. Clinical presentation is variable, ranging from asymptomatic cases to symptoms such as fatigue, dyspnea, palpitations, and chest pain (due to ischemia). Diagnosis is established through imaging methods such as echocardiography, cardiac computed tomography angiography, and coronary angiography. Currently, there are no standardized therapeutic guidelines for the management of CAF due to the rarity of cases. This article aims to report a case of a patient with CAF and complex coronary lesions who underwent coronary angioplasty and fistula embolization concomitantly.

Keywords: Fistula, Embryonic development, Left anterior descending artery, Right coronary artery.

INTRODUCTION

Perinatal Coronary artery fistulas (CAF) are rare congenital anomalies characterized by direct communications between one or more coronary arteries and cardiac chambers or adjacent great vessels. The prevalence of CAF is estimated at 0.2% to 0.4% of all congenital heart defects¹. Among the various forms of CAF, fistulas from the coronary artery to the pulmonary trunk (CAPF) are particularly uncommon, accounting for approximately 17% of CAF cases.²

The etiology of CAPF is predominantly attributed to abnormalities in the embryonic development process, specifically the persistence of embryonic myocardial sinusoids or incomplete involution of branches of the pulmonary sinus. The right coronary artery (RCA) and the left anterior descending artery (LAD) are the most frequently identified origins of these fistulas.¹

The clinical presentation of CAPF is highly variable, ranging from asymptomatic cases to nonspecific manifestations that resemble other heart diseases. When present, symptoms are

intrinsically related to the magnitude of blood flow shunting (left-to-right shunt) and the diameter of the fistula. Symptoms may include fatigue, exertional dyspnea, palpitations, chest pain (including myocardial ischemia due to the “coronary steal” phenomenon), and syncope.¹ It is noteworthy that syncope is an atypical manifestation and is rarely considered in the differential diagnosis of vascular malformations. On physical examination, most patients may not present significant findings; however, some may exhibit a continuous murmur suggestive of patent ductus arteriosus.

Regarding complementary examinations, the electrocardiogram rarely shows specific abnormalities. The diagnosis is primarily established through imaging methods such as echocardiography and cardiac computed tomography angiography. Coronary angiography is considered the gold standard for diagnostic confirmation and anatomical delineation of CAPF.¹

Currently, there are no standardized therapeutic guidelines for the management of CAPF.³ The scarcity of reported cases makes it difficult to establish universal management strategies. Therefore, the description of new cases significantly contributes to improving knowledge about the pathophysiology, clinical course, and potential complications of this condition, as well as assisting in the clarification of complex differential diagnoses.

The aim of this article is to report the case of a patient with complex obstructive coronary artery disease and multiple giant coronary fistulas to the pulmonary artery trunk, treated with coronary angioplasty associated with concomitant fistula embolization.

CASE REPORT

A 66-year-old female patient, with a history of systemic arterial hypertension, insulin-dependent diabetes mellitus, dyslipidemia, stage IV chronic kidney disease (non-dialysis), and pulmonary hypertension, was evaluated.

The initial diagnostic assessment, including myocardial perfusion scintigraphy, revealed significant ischemia (approximately 21%), with hypoperfusion involving the anterior, septal, and apical regions.

She underwent cardiac catheterization (CATH), which revealed heavily calcified lesions and significant obstructions: RCA: 90% proximal; LAD: 95% proximal and 90% in the mid segment (Figures 1A and 1C); left circumflex artery (LCx): 90% proximal; posterior descending artery (PDA): 80% in the mid segment. In addition, high-flow fistulas originating from the proximal segments of the LAD and RCA to the pulmonary trunk were identified (Figures 1B and 1D). Regarding pulmonary hypertension (pulmonary artery systolic pressure of 60 mmHg on CATH) and coronary-cameral fistulas, manometry performed during CATH revealed significant pulmonary arterial hypertension, and the presence of coronary-cameral fistulas was confirmed.

Given the patient's high surgical risk, the Heart Team decided on percutaneous treatment with coronary stenting and fistula embolization. The LAD was prepared with rotational atherectomy using a 1.5 mm burr, associated with a cutting balloon (Wolverine – Boston Scientific 3.5 × 15 mm) (Figure 1C and Figures 2A and 2B), followed by implantation of two everolimus-eluting stents (4.0 × 23 mm and 3.5 × 32 mm). The fistula originating from the LAD was embolized with 20 microcoils (Figure 2C).

In the same procedure, the RCA was selectively catheterized, and two guidewires were positioned: one along the fistula tract (Guidezilla 6F microcatheter) and another along the native coronary pathway (XB 3.5 6F guiding catheter). A 4 mm Amplatzer® AVP2 vascular plug was deployed in the proximal portion of the fistula, leaving treatment of the coronary lesion for a second stage, when complete occlusion of the malformation would be confirmed or not (Figure 2D).

Thirty days later, the patient returned for RCA stent implantation. Pre-intervention angiography

demonstrated unsuccessful fistula occlusion with a single device, with persistent high flow to the pulmonary trunk. We opted to treat the mid segment of the RCA, again using rotational atherectomy, followed by implantation of an initial stent in the mid segment (4.0 × 38 mm) to ensure adequate coronary flow.

Fistula embolization was then performed by crossing the previously implanted proximal plug with a guidewire (Hornet 0.14"), advancing the Guidezilla 6F microcatheter through the mesh of the plug into the mid segment of the fistula body, and deploying 8 microcoils, achieving complete occlusion confirmed by angiography. The microcatheter was then withdrawn to the proximal segment between the plug and the origin of the fistula, where 2 additional microcoils were released. Finally, a second stent (4.0 × 23 mm) was deployed in the proximal RCA with successful outcome (Figure 2D).

Reevaluation of the left coronary artery demonstrated complete occlusion of the arteriovenous fistula, with the LAD showing excellent flow and caliber. The patient remained hospitalized in the Intensive Care Unit after the procedure and was discharged the following day for outpatient follow-up.

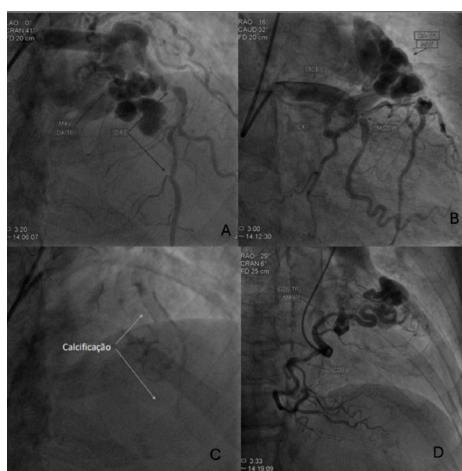


Figure 1: Angiographic images: 1A: Severe atherosclerotic coronary lesion in the left anterior descending artery. 1B: Fistula from the left anterior descending artery to the pulmonary artery trunk. 1C: Calcified atherosclerotic lesion in the left anterior descending artery. 1D: Fistula from the right coronary artery to the pulmonary artery trunk.

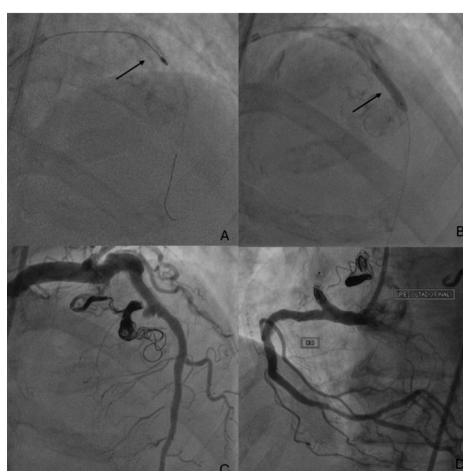


Figure 1: Angiographic images: 2A: Rotational atherectomy in an atherosclerotic lesion of the left anterior descending artery. 2B: Cutting balloon in the left anterior descending artery. 2C: Final result of left anterior descending artery angioplasty and fistula occlusion. 2D: Final result of right coronary artery angioplasty and fistula occlusion.

DISCUSSION

Coronary artery fistula to the pulmonary artery (CAPF) is a rare subtype, accounting for approximately 17% of all CAF cases.¹ Its incidence in the general population is estimated at 0.002%, with most cases being congenital. However, it may also be acquired due to trauma, iatrogenic coronary interventions, acute myocardial infarction, hypertrophic or dilated cardiomyopathy, and malignancy.⁴

Many patients with CAF are asymptomatic, especially those with small and hemodynamically insignificant shunts.³ However, the frequency of symptoms and complications increases with age, and the presentation of large fistulas in older individuals is extremely rare.⁴ The most common symptoms include angina (chest pain), dyspnea (shortness of breath), palpitations, dizziness, and syncope.² Angina may result from coronary artery disease (CAD) or from the coronary steal phenomenon.⁵ Coronary steal occurs when blood flow is diverted to a low-resistance receiving chamber (such as the pulmonary artery), leading to ischemia in myocardial regions with higher vascular resistance.

In a case reported by Saeed et al., myocardial ischemia resulting from coronary steal secondary to a fistula between the LAD and the pulmonary artery led to a non-ST-elevation myocardial infarction in a young patient.⁴ In our case report, the patient also presented significant ischemia on myocardial scintigraphy; however, with a multifactorial etiology related to the presence of obstructive coronary artery disease and the fistula.

The management of CAF remains controversial due to the rarity of cases and the lack of standardized treatment guidelines. The choice of therapy depends on the size of the fistula, its anatomical location, the patient's clinical presentation, and the presence of documented coronary steal.⁴ Therapeutic options include clinical management, surgical treatment, or transcatheter embolization.³

In a second case also reported by Saeed et al., the patient showed symptom improvement with clinical treatment alone, without the need for surgical or endovascular intervention.⁴ In contrast, in our case, the presence of significant ischemia associated with obstructive coronary artery disease precluded conservative management, leading to the decision to perform coronary angioplasty for the coronary obstruction and embolization with coils and a vascular plug due to the large-volume fistula in the LAD and RCA.

Surgical treatment remains the traditional gold standard and is considered a safe and effective option. It is performed via median sternotomy, with or without cardiopulmonary bypass.³ Surgical options include epicardial ligation, transection with closure of the opening, and drainage.³ The presence of a fistula requiring treatment demands evaluation by an experienced team, including cardiologists with expertise in congenital heart disease and a cardiac surgeon, to determine the best therapeutic approach.⁶

Direct comparative studies between surgical and endovascular treatment are still lacking, and both are considered viable therapeutic options. Percutaneous closure is preferred in cases of proximally originating fistulas with a single drainage site, whereas surgical treatment is generally reserved for distal fistulas and those with multiple drainage sites.⁴ In our case, given the presence of associated obstructive atherosclerotic coronary disease, the expertise of the Heart Team in percutaneous treatment of coronary and structural heart disease, and the patient's high surgical risk, a simultaneous percutaneous approach for both conditions was chosen.

CONCLUSION

Coronary artery fistulas to the pulmonary artery (CAPF) may represent a differential diagnosis in patients with acute or chronic coronary syndromes, mainly due to the coronary steal phenomenon, especially when associated with significant atherosclerotic disease. Mastery of multiple percutaneous intervention techniques

(used in endovascular surgery and neurointervention) allows, in selected cases, complete resolution of both the malformation and the atherosclerotic disease, particularly in patients with high surgical risk.

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ONCOPLASTIC BREAST SURGERY: ONCOLOGICAL SAFETY AND AESTHETIC OUTCOMES IN BREAST-CONSERVING TREATMENT

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ABSTRACT

Breast-conserving surgery has become the standard treatment for most patients with early-stage breast cancer after studies demonstrated outcomes equivalent to mastectomy regarding overall survival and local disease control. Despite its oncological effectiveness and psychosocial benefits, tumor excision may lead to significant breast deformities, particularly when lesions are located in critical breast regions. In this context, oncoplastic breast surgery emerged as an approach that combines oncologic surgical principles with reconstructive plastic surgery techniques, allowing wider resections while preserving breast aesthetics. Oncoplastic procedures are classified into volume displacement and volume replacement techniques, with the choice depending on tumor characteristics and patient anatomy. Current evidence supports the oncological safety of these procedures, showing recurrence rates comparable to conventional breast-conserving surgery, as well as lower rates of positive margins and reoperations. Improved cosmetic outcomes positively influence self-esteem, body image, sexuality, and overall quality of life. Furthermore, advances in neoadjuvant therapies have expanded the indications for breast-conserving approaches associated with oncoplastic techniques. Today, oncoplastic surgery is recognized as an essential component of modern breast cancer management, combining oncological safety with superior aesthetic outcomes and greater patient satisfaction.

Keywords: Breast cancer, Breast-conserving surgery, Oncoplastic surgery, Quality of life, Breast reconstruction.

INTRODUCTION

Breast-conserving surgery has become established, over recent decades, as one of the main therapeutic strategies in the treatment of early-stage breast cancer. The paradigm shift in surgical treatment occurred following prospective randomized studies conducted in the 1970s and 1980s, particularly those carried out by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and by the Milan group led by Umberto Veronesi. These studies demonstrated that breast-conserving surgery

combined with radiotherapy yielded outcomes equivalent to radical mastectomy in terms of overall survival and local disease control in appropriately selected patients. Since then, breast preservation has become the standard treatment for a large proportion of early-stage breast tumors.¹

In addition to its oncological efficacy, breast-conserving surgery has a positive impact on patients' quality of life. Breast preservation is associated with better body image perception, preservation of femininity, and lower levels of psychological distress when compared with total mastectomy. However, although oncologically safe, tumor resection alone may result in significant breast deformities, particularly when large volumes of glandular tissue need to be removed. Tumors located in the lower quadrants, central region, or medial pole of the breast frequently result in scar retraction, anatomical distortion, and marked asymmetry after adjuvant radiotherapy, compromising the final aesthetic outcome.²

In this context, oncoplastic breast surgery emerged, integrating the principles of oncological surgery with concepts of reconstructive plastic surgery. The term "oncoplasty" was introduced in the 1990s by Audretsch, proposing the combination of wide oncological resections with immediate breast remodeling techniques. This approach made it possible to expand the indications for breast-conserving surgery, including cases previously considered unsuitable for breast preservation due to an unfavorable tumor size-to-breast volume ratio.³

Oncoplastic breast surgery is based on two fundamental principles: oncological safety and aesthetic optimization. The first objective is to achieve adequate surgical margins, reducing the risk of local recurrence. The second aims to minimize deformities and improve breast symmetry through glandular remodeling and tissue redistribution techniques. Studies have demonstrated that oncoplastic techniques allow wider resections without increasing tumor recurrence rates, while also significantly reducing the need for reoperations due to involved margins.⁴

Oncoplastic techniques can be classified into tissue displacement ("volume displacement") and tissue replacement ("volume replacement") procedures. Displacement techniques use the remaining breast tissue to remodel the breast after tumorectomy and are particularly indicated for patients with medium-sized or large breasts and some degree of ptosis. Among the most commonly used methods are therapeutic mammoplasties using superior, inferior, or superomedial pedicles. Tissue replacement techniques, in turn, use locoregional autologous flaps, such as the lateral thoracodorsal flap and the latissimus dorsi myocutaneous flap, allowing extensive defects to be filled in patients with small breasts.⁵

The choice of oncoplastic technique should take multiple factors into consideration, including tumor location and size, breast volume, degree of ptosis, need for radiotherapy, presence of comorbidities, and the patient's aesthetic expectations. Individualized surgical planning is essential to achieve satisfactory outcomes, and a multidisciplinary approach involving breast surgeons, plastic surgeons, radiation oncologists, pathologists, and medical oncologists is frequently required.⁶

From an oncological standpoint, recent evidence reinforces the safety of oncoplastic surgery. De Lorenzi et al. (2016), in a multicenter study involving thousands of patients, demonstrated similar local recurrence rates between conventional breast-conserving surgery and oncoplastic techniques. Furthermore, the possibility of wider resections is associated with a reduction in positive margins, a factor directly related to fewer reoperations and improved locoregional control. A meta-analysis conducted by Losken et al. (2014) showed lower rates of margin involvement in patients undergoing oncoplastic surgery when compared with traditional breast-conserving surgery.^{6,7}

The aesthetic and psychosocial benefits are also widely described in the literature. Satisfactory cosmetic outcomes have a significant impact on patients' self-esteem, sexuality, and quality of life.

Studies using validated instruments, such as the BREAST-Q, demonstrate high levels of satisfaction after oncoplastic procedures, particularly when associated with contralateral symmetrization. In addition, patients undergoing oncoplastic surgery frequently exhibit better psychosocial adjustment and a lower perception of bodily mutilation.⁸⁻¹⁰

Another relevant aspect concerns the advances in neoadjuvant systemic therapies, which have further expanded the possibilities of breast-conserving surgery. Tumor reduction achieved with preoperative chemotherapy allows cases initially considered candidates for mastectomy to be converted to conservative approaches combined with oncoplastic surgery. This scenario reinforces the importance of multidisciplinary integration in the modern treatment of breast cancer.¹¹⁻¹⁴

Currently, oncoplastic surgery is considered a fundamental part of the contemporary management of breast cancer and should not be understood merely as a complementary aesthetic resource, but rather as a therapeutic strategy capable of combining oncological safety, functional preservation, and improved quality of life. Continuous technical development, associated with the increasing emphasis on patient-centered outcomes, has consolidated oncoplastic surgery as one of the pillars of modern breast surgery.^{15,16}

Fundamental Concepts of Oncoplastic Surgery

Oncoplastic breast surgery can be defined as the integration of the principles of oncological surgery and reconstructive plastic surgery techniques, with the aim of achieving adequate tumor resection while preserving the aesthetic and functional aspects of the breast. This approach seeks to ensure oncological safety without neglecting aspects related to the patient's body image, self-esteem, and quality of life.¹⁻⁵ The modern concept of oncoplastic surgery is based on the understanding that breast cancer treatment should not be restricted solely to local disease control but should also address the physical, emotional, and psychosocial impacts resulting from surgical treatment. Thus, oncoplastic surgery represents an evolution of traditional breast-conserving surgery, allowing wider resections with immediate reconstruction of the surgical defect.⁶⁻¹⁰ Oncoplastic surgery is based on several essential principles that guide the planning and performance of the surgical procedure.

Tumor Resection with Adequate Margins

The primary principle of oncoplastic surgery remains oncological safety. Tumor resection must follow the same technical criteria as conventional breast-conserving surgery, ensuring complete removal of the lesion with negative margins. Achieving adequate surgical margins significantly reduces the risk of local recurrence and the need for reoperations.¹¹⁻¹⁶

In this context, oncoplastic surgery offers an important advantage: the possibility of performing wider resections without compromising the final aesthetic outcome. This allows the breast surgeon greater surgical freedom, particularly in extensive tumors or tumors located in unfavorable regions of the breast. Studies have demonstrated lower rates of involved margins in oncoplastic procedures when compared with traditional breast-conserving surgery.

Three-Dimensional Planning of Resection

Unlike conventional lumpectomy, oncoplastic surgery requires detailed three-dimensional planning of breast resection. The surgeon must consider not only the size and location of the tumor but also anatomical factors related to breast shape, glandular volume, degree of ptosis, and position of the nipple-areola complex (NAC).

Tumor location directly influences the choice of reconstructive technique. Tumors located in the lower quadrants, for example, carry a greater risk of postoperative deformities, while central lesions often require specific approaches for preservation or reconstruction of the NAC. Preoperative planning includes a thorough clinical assessment, photographic documentation, and skin markings performed with the patient in the standing position.¹⁰⁻¹⁶

In addition, imaging examinations such as mammography, ultrasonography, and magnetic resonance imaging assist in accurately defining tumor extent and planning the resection.

Immediate Glandular Remodeling

After tumor removal, immediate remodeling of the remaining breast gland is performed. This principle constitutes one of the pillars of oncoplastic surgery and aims to prevent deformities secondary to the volume loss caused by resection.

Glandular remodeling may involve mobilization of local glandular flaps, rotation of breast segments, and tissue repositioning, allowing adequate filling of the surgical defect. Immediate reconstruction reduces scar retraction, contour irregularities, and anatomical distortions that tend to worsen after adjuvant radiotherapy.

Reorganization of breast tissue also promotes better distribution of scar tension, contributing to more durable aesthetic outcomes.⁶⁻⁹

Redistribution of the Remaining Breast Volume

Redistribution of the remaining breast tissue allows restoration of the natural breast shape after extensive resections. This concept is particularly important in tissue displacement (“volume displacement”) techniques, in which the breast tissue itself is used to remodel the breast.

Therapeutic mammoplasties represent a classic example of this principle and are frequently used in patients with breast hypertrophy or moderate to severe ptosis. In these situations, in addition to oncological treatment, the patient may obtain an additional functional benefit related to reduced breast weight and improvement in musculoskeletal symptoms.

When the residual volume is insufficient for adequate remodeling, locoregional autologous flaps may be used, characterizing tissue replacement (“volume replacement”) techniques.¹⁻⁴

Contralateral Symmetrization

Breast symmetry represents a fundamental component of the final aesthetic outcome. In many cases, particularly in therapeutic mammoplasties, a simultaneous approach to the contralateral breast becomes necessary to achieve better body balance.

Symmetrization procedures may include reduction mammoplasty, mastopexy, or volumetric adjustments of the opposite breast. In addition to the aesthetic benefit, symmetrization contributes to better psychosocial adjustment of the patient and greater satisfaction with treatment.

Several studies have demonstrated that immediate symmetrization is associated with better quality-of-life and body satisfaction scores, particularly when performed during the same surgical procedure as the oncological resection.¹⁻⁵

Preservation of the Vascular Supply to the Nipple-Areola Complex

Maintaining the viability of the nipple-areola complex (NAC) is a fundamental technical aspect of oncoplastic surgery. During surgical planning, the vascular pedicles responsible for the blood supply to the NAC must be

adequately preserved, minimizing the risk of necrosis, ischemic injury, and sensory changes.

The choice of pedicle depends on tumor location, the resection pattern, and the mammoplasty technique employed. Superior, inferior, medial, and superomedial pedicles may be used according to each clinical situation.

In addition to its aesthetic importance, preservation of the NAC has a strong psychological impact, since its integrity is closely related to the patient's perception of femininity and body identity.³⁻⁸

Integration of Oncological Safety and Aesthetic Outcomes

The main characteristic of oncoplastic surgery is the harmonious integration of oncological radicality and aesthetic preservation. Unlike the traditional view that prioritized tumor control exclusively, the contemporary approach recognizes that aesthetic and functional outcomes are also part of therapeutic success.

Thus, oncoplastic surgery should not be understood merely as a complementary reconstructive procedure, but rather as a comprehensive, patient-centered therapeutic strategy. The combination of oncological and reconstructive techniques allows for more individualized, safe, and less mutilating treatments, consolidating oncoplastic surgery as one of the pillars of modern breast cancer management.¹⁰

Indications for Oncoplastic Surgery in Breast-Conserving Surgery

Oncoplastic surgery is primarily indicated when conventional breast-conserving surgery presents a high risk of breast deformity, asymmetry, or an unsatisfactory aesthetic outcome. Its objective is to allow adequate oncological resections with negative margins, combined with immediate breast remodeling, preserving shape, volume, and symmetry.

The main indications include tumors that are proportionally large in relation to breast volume, lesions located in areas that are difficult to reconstruct aesthetically, the need for wide resections, medium-sized or large breasts, moderate or severe breast ptosis, pre-existing breast asymmetries, and patients who are candidates for adjuvant radiotherapy. International guidelines suggest considering oncoplastic techniques when resection exceeds approximately 20% of breast volume, when there is a full-thickness defect extending to the pectoral fascia, or when lumpectomy alone is likely to cause displacement of the nipple-areola complex.

The relationship between tumor volume and breast volume is one of the main factors in decision-making. Larger tumors, even when technically resectable, may produce significant retractions, depressions, and asymmetries after radiotherapy. In these cases, oncoplastic surgery allows wider resection and remodeling of the remaining parenchyma, reducing the risk of deformity. Clough et al. classify oncoplastic procedures according to levels of complexity, highlighting that smaller resections can be managed with simple remodeling, whereas more extensive resections generally require more elaborate mammoplasty techniques.

Tumor location is also a determining factor. Lesions in the lower quadrants, central region, medial pole, and junction of the inner quadrants carry a greater risk of deformities after conventional breast-conserving surgery. Central tumors may require partial or total resection of the nipple-areola complex, whereas tumors in the lower quadrants frequently cause inferior breast retraction and contour distortion. In these scenarios, the choice of mammoplasty pedicles, glandular flaps, or volume replacement techniques may better preserve breast shape.

Patients with medium-sized or large breasts and moderate or severe ptosis are particularly favorable candidates for tissue displacement techniques, such as therapeutic mammoplasties. These techniques allow tumor removal with wide margins, remodeling of the treated breast, and, when indicated, contralateral symmetrization during the same surgical procedure. In addition to the aesthetic benefit,

therapeutic breast reduction may improve symptoms related to breast hypertrophy, such as back pain, neck pain, and functional discomfort.

Oncoplastic surgery may also be indicated in selected cases of extensive ductal carcinoma in situ, limited multifocal or multicentric tumors, carefully selected local recurrence, and deformities following previous quadrantectomy. However, these indications require individualized assessment, with correlation between clinical examination, mammography, ultrasonography, magnetic resonance imaging when necessary, and multidisciplinary discussion. The international consensus conference on oncoplastic breast-conserving surgery reinforces the need for standardization of indications, surgical planning, and evaluation of oncological and aesthetic outcomes.

From an evidence-based perspective, oncoplastic surgery is associated with a reduction in involved margins, a lower need for reoperations, and a lower rate of conversion to mastectomy compared with conventional breast-conserving surgery. A meta-analysis reported a rate of positive or close margins of 12.3% in patients undergoing oncoplastic surgery, lower than that observed with traditional breast-conserving surgery in some series. Reviews and population-based studies also indicate a modest reduction in re-excision rates and a lower frequency of conversion to mastectomy after oncoplastic surgery.⁶⁻¹²

Contraindications

Despite its broad applicability, oncoplastic breast-conserving surgery should not be performed when it compromises oncological safety. The main absolute contraindication is the inability to achieve negative margins without excessive removal of breast volume. In this situation, mastectomy should be considered the safest alternative.

Other absolute contraindications include extensive prior breast radiotherapy, inflammatory breast disease, diffuse microcalcifications suspicious for extensive involvement, T4 tumors, and a tumor-to-breast ratio incompatible with an acceptable aesthetic outcome. Reviews of oncoplastic breast-conserving surgery reinforce that breast conservation is contraindicated when negative margins cannot be ensured, in T4 tumors, and in inflammatory disease.

Relative contraindications include heavy smoking, morbid obesity, uncontrolled diabetes, collagen vascular diseases, extensive multicentric tumors, and poor adherence to adjuvant treatment. These factors do not necessarily preclude surgery but increase the risk of complications, such as skin necrosis, ischemia of the nipple-areola complex, infection, dehiscence, seroma, and delay in the initiation of adjuvant radiotherapy.

Smoking deserves particular attention because it compromises microcirculation and wound healing, increasing the risk of flap and nipple-areola complex necrosis. Obesity and uncontrolled diabetes also increase the risk of infection and surgical wound complications. Collagen vascular diseases, in turn, may impair healing and increase radiotherapy-related toxicity, requiring joint assessment with medical oncology and radiation oncology.

Finally, poor adherence to adjuvant treatment constitutes an important relative contraindication, since breast-conserving surgery depends on the appropriate completion of adjuvant radiotherapy and oncological follow-up. Thus, the indication for oncoplastic surgery should always consider not only the technical feasibility of surgery but also the patient's clinical, social, and therapeutic context.^{6,7}

Classification of Oncoplastic Techniques

Oncoplastic techniques used in breast-conserving surgery can be classified into two major groups: volume displacement techniques ("volume displacement") and volume replacement techniques

("volume replacement"). This classification is based on how the surgical defect is reconstructed after tumor resection and constitutes one of the pillars of reconstructive planning in oncoplastic surgery.

The choice between one modality and the other depends on several factors, including breast volume, tumor-to-breast ratio, lesion location, degree of ptosis, need for wide resections, and the experience of the surgical team. Both strategies aim to preserve oncological safety while simultaneously optimizing aesthetic and functional outcomes.¹⁻³

Volume Displacement Techniques

Volume displacement techniques are based on the mobilization, rotation, and redistribution of residual breast tissue to fill the defect created by tumor resection. These techniques use exclusively the breast's own tissue for glandular remodeling, without the need to transfer tissue from other regions of the body.

They are particularly indicated in patients with medium-sized or large breasts, especially when there is moderate or severe breast ptosis. In these cases, there is sufficient glandular tissue to allow adequate remodeling after lumpectomy. In general, these techniques are recommended when the resection corresponds to approximately 20% to 30% of breast volume, although more complex procedures may allow even larger resections in selected situations.

In addition to reconstruction of the surgical defect, displacement techniques frequently provide an overall aesthetic improvement of the breast and may correct breast hypertrophy, sagging, and pre-existing asymmetries. The combination with contralateral symmetrization procedures contributes to better cosmetic outcomes and greater patient satisfaction.

Clough et al. proposed a classification of oncoplastic techniques based on the resected volume and reconstructive complexity. Level I procedures involve smaller resections with simple remodeling, whereas Level II procedures include larger resections associated with more elaborate therapeutic mammoplasty techniques.⁶⁻¹²

Main Indications

Volume displacement techniques are most indicated in:

- Medium-sized or large breasts;
- Patients with moderate or severe breast ptosis;
- Need for resection of up to 20–30% of breast volume;
- Tumors located in regions amenable to glandular remodeling;
- Patients who are candidates for therapeutic reduction mammoplasty;
- Cases in which breast symmetrization is desired.

Advantages

The main advantages of these techniques include:

- Use of autologous tissue from the breast itself;
- Better texture and consistency of the reconstruction;
- Lower donor-site morbidity;
- Possibility of immediate symmetrization;
- Frequently superior aesthetic outcomes;
- Simultaneous correction of breast ptosis.

However, these techniques may not be suitable for patients with small breasts or very extensive

defects, in which the residual volume is insufficient for adequate remodeling.

Therapeutic Reduction Mammoplasty

Therapeutic reduction mammoplasty represents one of the most commonly used techniques in oncoplastic surgery. It consists of the combination of oncological quadrantectomy and conventional reduction mammoplasty techniques.

The tumor is incorporated into the mammoplasty resection pattern, allowing wide glandular resection and simultaneous breast remodeling. The choice of vascular pedicle for the nipple-areola complex depends on tumor location and the planned reduction pattern.

This technique provides excellent outcomes in patients with breast hypertrophy, providing not only adequate oncological control but also functional improvement related to the reduction in breast weight.¹⁻⁵

Oncoplastic Mastopexy

Oncoplastic mastopexy uses principles similar to those of aesthetic mastopexy to remodel the breast after tumor resection. It is particularly indicated in patients with moderate ptosis and preserved breast volume.

In addition to reconstruction of the defect, it promotes repositioning of the nipple-areola complex and improvement of breast contour.

Local Glandular Flaps

Local glandular flaps consist of the mobilization of segments of adjacent breast parenchyma to fill the surgical defect. They are widely used in smaller resections and localized defects.

They may be used alone or in combination with more complex mammoplasty techniques.

Volume Replacement Techniques

Volume replacement techniques use autologous tissues from regions adjacent to or distant from the breast to reconstruct the surgical defect. Unlike displacement techniques, in these situations the lost volume is replaced with tissue from outside the breast.

They are particularly indicated in patients with small breasts, limited glandular tissue availability, or a need for extensive resections. They also play an important role in defects located in specific quadrants that are difficult to remodel, particularly the lateral and lower quadrants and the central region.

These techniques allow the indications for breast-conserving surgery to be expanded even in situations in which glandular remodeling alone would be insufficient.^{6,7}

Main Indications

Volume replacement techniques are most indicated in:

- Small breasts;
- Extensive resections;
- Unfavorable tumor-to-breast ratio;
- Defects located in specific quadrants;
- Patients without an indication for reduction mammoplasty;
- Selected cases of local recurrence.

Advantages

The main advantages include:

- Possibility of breast preservation in extensive defects;
- Better volume replacement;
- Less distortion of the residual breast;
- Applicability in thin patients or those with low glandular volume.

However, these techniques are associated with greater surgical complexity and a potential increase in donor-site morbidity.

Latissimus Dorsi Muscle Flap

The latissimus dorsi myocutaneous flap is one of the most traditional volume replacement techniques. It uses muscle, subcutaneous tissue, and, when necessary, skin from the dorsal region to fill the breast defect.

It has a reliable blood supply and great reconstructive versatility, being particularly useful for extensive defects of the lateral breast quadrants.

Lateral Thoracodorsal Flap

The lateral thoracodorsal flap uses lateral adipocutaneous tissue from the chest wall for partial breast volume replacement. It is a less invasive technique than the classic latissimus dorsi flap, with lower functional morbidity.

Lateral Intercostal Flap

The lateral intercostal flap is based on the blood supply from the lateral intercostal vessels. It allows reconstruction of defects located mainly in the lateral and lower quadrants.

LICAP (Lateral Intercostal Artery Perforator)

The LICAP flap uses perforators of the lateral intercostal artery without the need to sacrifice muscle. It is a modern technique for partial breast reconstruction with lower morbidity and better functional preservation.

The LICAP flap provides good outcomes in lateral breast defects and has gained widespread acceptance due to less postoperative pain and reduced functional impairment.

TDAP (Thoracodorsal Artery Perforator)

The TDAP flap uses perforators of the thoracodorsal artery while preserving the latissimus dorsi muscle. It constitutes a less invasive alternative to the classic muscle flap, reducing donor-site morbidity.

It offers excellent reconstructive versatility and good cosmetic outcomes, particularly in moderate defects of the lateral breast.

Preoperative Planning in Oncoplastic Surgery

Preoperative planning constitutes one of the most important stages of oncoplastic breast surgery. Unlike conventional breast-conserving surgery, the oncoplastic approach requires detailed integration of oncological, anatomical, and reconstructive principles, making an individualized and multidisciplinary assessment essential.

The success of surgery depends not only on adequate tumor resection but also on the ability to predict the volumetric and aesthetic impact of the resection on the breast. Thus, adequate preoperative

planning is directly related to achieving negative surgical margins, reducing reoperation rates, preserving breast symmetry, and improving patient satisfaction.

Several studies have demonstrated that failures in preoperative planning are associated with higher rates of aesthetic deformities, asymmetries, and the need for delayed corrective procedures. Therefore, oncoplastic surgery requires careful assessment of the patient, the tumor, and reconstructive options even before the surgical incision.⁵⁻¹⁰

Clinical Assessment

Clinical assessment represents the first step in oncoplastic planning. It should be performed thoroughly, considering the anatomical characteristics of the breast, oncological factors, and the patient's individual expectations.

Breast Volume

Breast volume plays a central role in defining the reconstructive strategy. Patients with medium-sized or large breasts generally have greater availability of glandular tissue, favoring volume displacement techniques, such as therapeutic mammoplasties and oncoplastic mastopexies.

Patients with small breasts, on the other hand, have less tissue reserve, making volume replacement techniques with autologous flaps more frequently necessary. The relationship between tumor volume and breast volume is considered one of the main determinants of the risk of postoperative deformity.

Studies have demonstrated that resections exceeding approximately 20% of breast volume are associated with poorer aesthetic outcomes when not accompanied by adequate oncoplastic remodeling.⁴⁻⁹

Degree of Ptosis

The degree of breast ptosis directly influences the choice of reconstructive technique. Patients with moderate or severe ptosis frequently benefit from therapeutic mammoplasties, allowing simultaneous oncological treatment, breast remodeling, and overall aesthetic improvement.

Assessment of ptosis also assists in determining the vascular pedicle of the nipple-areola complex (NAC), planning the incisions, and determining the need for contralateral symmetrization.

Tumor-to-Breast Ratio

The ratio between tumor size and breast volume is one of the main criteria for indicating oncoplastic breast-conserving surgery. Relatively large tumors in small breasts carry a greater risk of deformity and may require more complex reconstructive techniques.

This assessment should consider not only tumor diameter but also the three-dimensional extent of the resection, the need for wider margins, and the potential impact of radiotherapy on the residual breast.

Tumor Location

Tumor location significantly influences the cosmetic outcome and the choice of surgical technique. Lesions in the lower quadrants, central region, and medial pole have a greater potential for aesthetic distortion after conventional breast-conserving surgery.

Central tumors frequently require reconstruction of the NAC, whereas lateral lesions can be more easily approached using local flaps or glandular techniques.

Clough et al. developed a quadrant-by-quadrant atlas relating tumor location to specific oncoplastic strategies, emphasizing the importance of individualized anatomical planning.

Comorbidities

The presence of comorbidities should be carefully assessed due to their impact on wound healing, tissue vascularization, and the risk of complications.

The most relevant factors include:

- Smoking;
- Diabetes mellitus;
- Obesity;
- Arterial hypertension;
- Collagen vascular diseases;
- Cardiovascular diseases;
- Chronic corticosteroid use.

Patients who smoke have a higher risk of skin necrosis and vascular compromise of the NAC. Obesity and diabetes are also associated with an increased risk of infectious complications and surgical wound dehiscence.

Patient Expectations

Oncoplastic surgery should be patient-centered, and understanding the patient's expectations regarding treatment, breast shape, scars, and body symmetry is essential.

Informed consent should include a detailed discussion of:

- Possibility of residual asymmetry;
- Need for contralateral symmetrization;
- Possible future surgical revisions;
- Impact of radiotherapy;
- Expected scars;
- Risks and complications.

Studies using instruments such as the BREAST-Q demonstrate that adequate alignment between expectations and surgical outcomes is strongly associated with postoperative satisfaction.

Radiological Assessment

Imaging assessment is essential in the planning of oncoplastic surgery, allowing precise definition of tumor extent and assisting in the choice of reconstructive technique.

Mammography

Mammography remains a fundamental examination in the preoperative assessment. It allows identification of tumor extent, the presence of microcalcifications, multifocality, and multicentricity.

In addition, it assists in determining the relationship between the tumor and important anatomical structures, such as the nipple-areola complex.

Ultrasonography

Ultrasonography complements mammography, particularly in dense breasts. It allows a more detailed assessment of tumor dimensions, the relationship with deep tissue planes, and the

evaluation of suspicious axillary lymph nodes.

It also plays an important role in the preoperative localization of non-palpable lesions.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) has high sensitivity in the assessment of tumor extent and is particularly useful in selected situations, such as:

- Dense breasts;
- Invasive lobular tumors;
- Suspected multifocality;
- Assessment after neoadjuvant chemotherapy;
- Planning of complex cases.

However, indiscriminate use of MRI may increase mastectomy rates without a proven survival benefit; therefore, its indication should be individualized.

Preoperative Tumor Localization

Preoperative localization is essential for non-palpable lesions. Techniques such as wire-guided localization, radioactive localization, magnetic seeds, and radar markers allow precise localization of the lesion during surgery.

Adequate tumor localization reduces the risk of involved margins and minimizes excessive removal of healthy tissue.

Aesthetic Planning

Oncoplastic surgery requires aesthetic planning as rigorous as oncological planning. The objective is to minimize deformities and preserve body harmony.

Affected Quadrant

Each breast quadrant presents specific reconstructive challenges. Tumors in the lower quadrants generally require more elaborate mammoplasty techniques due to the greater risk of retraction.

Lateral lesions can frequently be treated with local flaps or less complex techniques.

Amount of Tissue to Be Removed

Volumetric estimation of the resection directly influences the choice of reconstructive technique. Small defects can be corrected with simple remodeling, whereas larger defects frequently require therapeutic mammoplasties or volume replacement flaps.

Contralateral Symmetry

Symmetrization of the contralateral breast may be performed during the same surgical procedure to improve body balance and aesthetic satisfaction.

The most common procedures include:

- Mastopexy;
- Reduction mammoplasty;
- Volume adjustments.

The decision should consider the patient's preference, pre-existing asymmetry, and the impact

of radiotherapy on the treated breast.

Planned Scars

The positioning of incisions should simultaneously consider adequate oncological access and cosmetic outcome. Scars should be strategically planned, respecting skin tension lines and the principles of mammoplasty techniques.

“Inverted-T,” vertical, periareolar, and lateral patterns may be used according to the technique selected.

Oncoplastic Techniques by Breast Quadrant

Tumor location represents one of the main determining factors in the planning of oncoplastic breast surgery. Each breast quadrant has specific anatomical characteristics related to glandular distribution, vascularization, tissue mobility, and the aesthetic impact of resection. Thus, the choice of reconstructive technique should be individualized according to the affected quadrant, aiming to preserve breast symmetry, minimize deformities, and ensure adequate oncological safety.

Clough et al. proposed an important quadrant-by-quadrant atlas for oncoplastic surgery, demonstrating that certain techniques provide better outcomes according to tumor location. Understanding these anatomical particularities allows optimization of surgical planning and reduction of late aesthetic complications.⁵⁻¹⁰

Upper Quadrants

The upper quadrants of the breast generally provide better conditions for breast-conserving surgery due to greater glandular mobility and the possibility of more favorable tissue redistribution. The greater volume in the upper pole facilitates remodeling after tumor resection, frequently resulting in better cosmetic outcomes.

In addition, scars located in the upper quadrants tend to be less noticeable and less susceptible to visible retraction after radiotherapy.

Techniques Used

Simple Glandular Remodeling

Simple glandular remodeling consists of mobilizing adjacent breast tissue to fill the surgical defect. It is particularly useful for small or moderate resections located in the upper outer quadrants. This technique has low morbidity and preserves the natural contour of the breast.

Superior Pedicle

The superior pedicle is widely used in therapeutic mammoplasties for tumors located in the lower or central regions, preserving the blood supply to the nipple-areola complex through the superior vascular supply.

It provides good vascular viability and adequate glandular mobility.

Round Block Technique

The round block technique allows wide periareolar access with excellent scar camouflage. It is particularly useful for upper lesions close to the NAC and for small to moderate tumors.

Periareolar Mastopexy

Periareolar mastopexy may be used to correct minor deformities and reposition the nipple-areola complex after upper resections.

Lower Quadrants

The lower quadrants represent one of the most challenging regions in breast-conserving surgery. Tumor resection in this location frequently results in retraction of the lower pole, a deformity known as “bird beak deformity,” elevation of the inframammary fold, and distortion of the breast contour. These deformities tend to worsen after radiotherapy due to tissue fibrosis.

For this reason, tumors in the lower quadrants frequently require more elaborate oncoplastic techniques.

Techniques Used

Therapeutic Mammoplasty

Therapeutic mammoplasty is considered one of the best options for lower defects, allowing wide glandular resection combined with immediate breast remodeling.

Patients with medium-sized or large breasts and breast ptosis achieve excellent outcomes with this approach.

Superior or Superomedial Pedicle

The use of superior or superomedial pedicles allows better filling of the lower pole after tumor resection. These techniques favor maintenance of breast projection and adequate vascularization of the NAC.

The superomedial pedicle has gained prominence due to its good mobility, vascular safety, and consistent aesthetic outcomes.

Local Flaps

In extensive defects or patients with lower breast volume, local adipocutaneous flaps may be used for additional filling of the lower defect.

Medial Quadrants

The medial quadrants represent an important reconstructive challenge due to the risk of breast cleavage asymmetry. Small deformities in this region become easily noticeable due to the central position of the breast.

In addition, medial scars tend to be more visible and may significantly compromise the aesthetic outcome.

Reconstructive Options

Rotational Glandular Flaps

Rotational mobilization of adjacent breast tissue allows filling of the medial defect while preserving the inner contour of the breast.

These flaps provide good outcomes in small and moderate defects.

Periareolar Techniques

Periareolar techniques provide adequate aesthetic access for lesions close to the nipple-areola complex, reducing scar visibility.

The round block technique is particularly useful for medial periareolar lesions.

Local Chest Wall Flaps

In larger defects, adipocutaneous flaps from the medial chest wall may be used to replace the lost volume.

Lateral Quadrants

The lateral quadrants generally provide better conditions for reconstruction due to the greater availability of lateral tissue and proximity to the chest wall.

These regions are particularly suitable for perforator flaps and volume replacement techniques.

Techniques Used

LICAP (Lateral Intercostal Artery Perforator)

The LICAP flap uses perforators from the lateral intercostal arteries for the reconstruction of lateral breast defects.

It is a modern and widely used technique due to the following advantages:

- Muscle preservation;
- Low morbidity;
- Good mobility;
- Less postoperative pain;
- Functional preservation.

Studies have demonstrated good cosmetic outcomes and low donor-site morbidity.

Lateral Thoracodorsal Flap

The lateral thoracodorsal flap uses lateral adipocutaneous tissue without the need for extensive muscle dissection. It is useful for moderate defects of the lateral quadrants.

Lateral Glandular Advancement

Advancement of the lateral glandular tissue allows small defects to be filled without the need for additional flaps.

Therapeutic Mammoplasty

Therapeutic mammoplasty represents one of the most widely used and studied techniques in modern oncoplastic surgery. It consists of the combination of wide tumor resection with reduction mammoplasty or mastopexy techniques.

This approach allows:

- Wider surgical margins;
- Immediate breast remodeling;
- Bilateral symmetrization;
- Correction of breast ptosis;
- Preservation of breast shape.

Advantages

Several studies have demonstrated important benefits of therapeutic mammoplasty.

Excellent Aesthetic Outcome

Immediate breast remodeling reduces deformities and improves body symmetry.

Better Radiotherapy Distribution

Glandular reorganization promotes a more homogeneous distribution of the radiotherapy dose, reducing localized retractions.

Functional Benefit in Macromastia

Patients with breast hypertrophy frequently experience improvement in:

- Neck pain;
- Back pain;
- Shoulder grooves;
- Postural limitations.

Lower Reoperation Rates

The possibility of wider resections reduces the rates of involved margins.

Meta-analyses have demonstrated lower re-excision rates compared with conventional breast-conserving surgery.

Disadvantages

Despite the benefits, some limitations should be considered:

- Longer operative time;
- Extensive scars;
- Possibility of NAC necrosis;
- Sensory changes;
- Greater technical complexity.

Vascular complications of the NAC are more frequent in patients who smoke, are obese, or have diabetes.

Round Block Technique

The round block technique, described by Benelli, represents an important option for central or periareolar tumors.

It is based on:

- Double periareolar incision;
- Extensive glandular dissection;
- Centripetal remodeling;
- Excellent scar camouflage.

Indications

The technique provides better outcomes in:

- Small tumors;
- Small or medium-sized breasts;
- Lesions close to the NAC;
- Patients with mild ptosis.

Advantages

- Minimally visible scar;
- Good symmetry;

- Aesthetic preservation of the breast;
- Wide surgical access for central tumors.

Limitations

The technique has limitations in:

- Extensive resections;
- Severely ptotic breasts;
- Peripheral tumors;
- Large glandular defects.

In these situations, areolar widening, breast flattening, or residual deformity may occur.

Local and Perforator Flaps

The evolution of perforator flaps has revolutionized contemporary oncoplastic surgery. These techniques allow volume reconstruction with lower functional morbidity, preserving muscles and reducing donor-site complications.

LICAP

The LICAP flap is based on lateral intercostal perforator vessels and has become one of the main options for partial reconstruction of the lateral breast.

Advantages

- Muscle preservation;
- Low morbidity;
- Good mobility;
- Less postoperative pain;
- Faster functional recovery.

It provides excellent outcomes in lateral and lower defects.

TDAP

The TDAP flap uses thoracodorsal artery perforators without the need to sacrifice the latissimus dorsi muscle.

This technique offers:

- Less pain;
- Functional preservation;
- Lower dorsal morbidity;
- Good reconstructive volume;
- Better postoperative recovery.

Currently, the TDAP is considered a modern alternative to the classic latissimus dorsi flap in selected cases.

Surgical Margins and Oncological Safety

Oncological safety constitutes the fundamental principle of oncoplastic breast surgery. Although oncoplastic surgery is distinguished by the combination of oncological treatment and immediate aesthetic reconstruction, no cosmetic benefit should compromise the surgical radicality required for

adequate local disease control. Thus, the same oncological principles applied to conventional breast-conserving surgery must be rigorously observed during oncoplastic procedures.

Historically, there was concern that immediate breast remodeling could hinder the pathological assessment of margins, compromise future reoperations, or increase the risk of local recurrence. However, prospective studies, systematic reviews, and international consensus statements have demonstrated that, when properly performed by trained teams, oncoplastic surgery provides oncological safety comparable to conventional breast-conserving surgery, in addition to advantages related to lower rates of involved margins and a reduced need for reoperations.^{6,7}

Fundamental Oncological Objectives

Oncoplastic surgery must adhere to the classic principles of breast oncological surgery, including:

- Complete resection of the lesion;
- Achievement of negative surgical margins;
- Adequate anatomical orientation of the surgical specimen;
- Radiological and pathological correlation;
- Adequate axillary staging when indicated;
- Integrated planning with radiotherapy and systemic therapies.

The primary objective remains local disease control, with the aesthetic outcome considered a complementary benefit rather than a substitute for oncological safety.

Complete Resection of the Lesion

Complete tumor resection represents the main determinant of the effectiveness of breast-conserving surgery. In oncoplastic surgery, the possibility of immediate remodeling allows the surgeon to perform wider resections without concern for significant aesthetic deformity.

This aspect constitutes one of the greatest advantages of modern oncoplastic surgery, particularly in larger tumors or tumors located in regions traditionally considered unfavorable for breast-conserving surgery.

Studies have demonstrated that oncoplastic techniques frequently allow the removal of a greater volume of glandular tissue compared with conventional lumpectomy, reducing the risk of positive margins.

In addition, the freedom to widen the margins may reduce the need for conversion to mastectomy in selected cases.^{6,10}

Negative Surgical Margins

Achieving negative margins is one of the main factors associated with reducing local recurrence in breast cancer. According to the current consensus of the Society of Surgical Oncology (SSO) and the American Society for Radiation Oncology (ASTRO), an adequate margin for invasive carcinoma is defined as the absence of tumor on ink ("no ink on tumor").

For ductal carcinoma in situ (DCIS), margins of at least 2 mm are generally recommended to reduce the risk of local recurrence.

In oncoplastic surgery, the possibility of wider resections favors the achievement of adequate margins. Several series have demonstrated lower rates of involved margins compared with conventional breast-conserving surgery.

A meta-analysis published by Losken et al. found lower re-excision rates in patients undergoing oncoplastic surgery, suggesting an oncological benefit associated with wider resections.

Anatomical Orientation of the Surgical Specimen

Adequate anatomical orientation of the surgical specimen is an essential step in oncoplastic surgery. After wide resections and glandular remodeling, it becomes extremely difficult to identify the tumor bed if margin re-excision is required.

For this reason, the surgical specimen should be carefully oriented with sutures, clips, or anatomical markers, identifying:

- Superior margin;
- Inferior margin;
- Medial margin;
- Lateral margin;
- Deep margin;
- Superficial margin.

Effective communication among the surgeon, radiologist, and pathologist is essential for the correct interpretation of the margins.

In addition, the placement of metallic clips in the tumor bed assists in planning adjuvant radiotherapy, particularly in the administration of a “boost” to the area at greatest risk.

Radiological and Pathological Correlation

The correlation between radiological and pathological findings is critically important in oncoplastic breast-conserving surgery.

This process involves:

- Confirmation of complete removal of the lesion;
- Assessment of microcalcifications;
- Verification of margins;
- Correlation among clinical, radiological, and pathological tumor size.

In non-palpable lesions, intraoperative radiography of the surgical specimen is an important tool for ensuring complete inclusion of the tumor target.

In cases of DCIS or multifocal tumors, this step becomes even more relevant due to the greater risk of underestimating the extent of the disease.

Impact of Oncoplastic Surgery on Surgical Margins

Several studies have demonstrated that oncoplastic surgery is associated with reduced rates of positive margins and a consequent decrease in the need for reoperations.

This advantage results mainly from:

- Greater freedom to perform wide resections;
- Better three-dimensional planning;
- Less concern regarding immediate aesthetic deformity;
- Possibility of simultaneous reconstruction.

Fitoussi et al., in an analysis of 540 consecutive cases of oncoplastic surgery, demonstrated low rates of involved margins associated with good aesthetic outcomes.

In addition, recent population-based studies suggest a lower rate of secondary mastectomy in patients undergoing oncoplastic surgery.

Need for Reoperations

The presence of positive margins frequently requires a new surgical intervention, increasing morbidity, costs, and psychological impact.

Oncoplastic surgery offers a potential benefit in reducing reoperations due to the possibility of a wider initial resection.

Reoperations after glandular remodeling may be technically more complex due to the altered anatomy of the breast. Therefore, adequate initial planning and the achievement of negative margins become even more important.

The literature consistently demonstrates lower re-excision rates with oncoplastic techniques compared with traditional breast-conserving surgery.

Local Recurrence and Survival

One of the main concerns related to oncoplastic surgery is the risk of local recurrence. However, current evidence demonstrates recurrence rates similar to those observed with conventional breast-conserving surgery.

De Lorenzi et al., in a study involving a large number of patients with long-term follow-up, observed comparable oncological safety between oncoplastic surgery and traditional breast-conserving surgery. Likewise, systematic reviews and meta-analyses have demonstrated no adverse impact on:

- Overall survival;
- Disease-free survival;
- Locoregional control.

These findings reinforce that oncoplastic surgery represents an oncologically safe technique when performed with appropriate patient selection.

Radiotherapy after Oncoplastic Surgery

Adjuvant radiotherapy remains a fundamental component of breast-conserving treatment for breast cancer, including after oncoplastic procedures. Its main purpose is to reduce the risk of local recurrence, contributing significantly to locoregional disease control and improved long-term survival rates.

Several landmark studies have demonstrated that the combination of breast-conserving surgery and radiotherapy provides oncological efficacy equivalent to mastectomy in appropriately selected patients. Thus, even after complex oncoplastic reconstructions, radiotherapy continues to be considered mandatory for most patients undergoing breast preservation.

However, oncoplastic surgery introduces new challenges for radiotherapy planning, mainly due to the anatomical changes resulting from glandular remodeling. Redistribution of breast tissue may alter the original location of the tumor bed, making precise delineation of the area at greatest risk for local recurrence more difficult.

For this reason, multidisciplinary integration among the breast surgeon, radiation oncologist, radiologist, and pathologist has become an essential element in ensuring adequate delivery of radiotherapy after oncoplastic surgery.^{6,7}

Importance of Radiotherapy in Breast-Conserving Surgery

Radiotherapy after breast-conserving surgery significantly reduces local recurrence rates and improves long-term oncological outcomes.

Meta-analyses by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) have demonstrated that radiotherapy after breast-conserving surgery reduces the risk of local recurrence by approximately half and contributes to a reduction in breast cancer-specific mortality.

Thus, oncoplastic procedures do not eliminate the need for radiotherapy, even in cases with excellent surgical margins or a favorable pathological response.

The indication for radiotherapy should follow the same principles as those applied to conventional breast-conserving surgery.

Challenges of Radiotherapy after Oncoplastic Surgery

Although oncoplastic surgery provides important aesthetic and functional benefits, breast remodeling may create technical difficulties in radiotherapy planning.

The main challenges include:

- Identification of the tumor bed;
- Anatomical changes in the breast;
- Glandular redistribution;
- Displacement of the original resection site;
- Changes in breast contour;
- Difficulty in administering the "boost."

These changes make adequate intraoperative planning and communication among the teams involved essential.

Tumor Bed Localization

Accurate identification of the tumor bed constitutes one of the main challenges of radiotherapy after oncoplastic surgery.

In conventional breast-conserving surgery, the lumpectomy bed generally remains relatively anatomically preserved. However, in oncoplastic surgery, significant mobilization of breast tissue occurs, which may completely displace the original resection area.

This situation makes the following more difficult:

- Delineation of the radiotherapy boost area ("boost");
- Planning of radiation fields;
- Interpretation of postoperative images.

This difficulty becomes even greater with therapeutic mastopexy techniques and extensive glandular remodeling.

Studies have demonstrated that failure to adequately identify the tumor bed may compromise the accuracy of the "boost" and potentially increase the risk of local failure.

Need for Surgical Clips

The placement of metallic surgical clips in the tumor bed currently represents one of the most important measures for adequate radiotherapy planning after oncoplastic surgery.

The clips serve as radiopaque anatomical markers, allowing precise identification of the resected area during computed tomography-based radiotherapy planning.

The placement of multiple clips at the margins of the tumor bed is recommended, generally including:

- Superior margin;

- Inferior margin;
- Medial margin;
- Lateral margin;
- Deep margin.

Adequate three-dimensional marking significantly assists the radiation oncologist in delineating the target volume.

International consensus statements reinforce the importance of systematic clip placement in oncoplastic procedures due to the anatomical changes caused by breast remodeling.

Changes in Dose Distribution

Breast remodeling modifies the geometry of the irradiated breast and may alter radiotherapy dose distribution.

The main factors involved include:

- Glandular redistribution;
- Changes in breast shape;
- Volume reduction;
- Displacement of the tumor bed;
- Changes in tissue thickness.

These changes may influence:

- Dose homogeneity;
- Target volume coverage;
- Skin toxicity;
- Late fibrosis;
- Final aesthetic outcome.

However, some studies suggest that therapeutic mammoplasty may promote a more homogeneous distribution of radiation due to improved breast shape after remodeling.

In addition, reduction in breast volume may decrease areas of dose overlap and reduce skin toxicity in patients with macromastia.

Radiotherapy Boost

The “boost” consists of an additional dose of radiation administered specifically to the tumor bed, with the aim of reducing the risk of local recurrence.

After oncoplastic surgery, boost planning becomes more complex due to the difficulty in anatomically identifying the original tumor bed.

Correct intraoperative marking with metallic clips plays an essential role in this context.

Some authors suggest caution when administering extensive boosts after major glandular remodeling due to the potential negative aesthetic impact, including:

- Localized fibrosis;
- Breast retraction;
- Late asymmetry;
- Changes in texture.

The decision should be individualized according to age, margins, tumor subtype, and risk factors

for local recurrence.

Postoperative Radiological Changes

Oncoplastic surgery produces complex radiological changes that may make interpretation of follow-up imaging more difficult.

Common findings include:

- Areas of fibrosis;
- Fat necrosis;
- Architectural distortion;
- Benign calcifications;
- Glandular asymmetries.

These changes may mimic tumor recurrence, making prior knowledge of the surgical technique used important.

Detailed surgical documentation and communication between the breast surgeon and radiologist significantly assist in the appropriate interpretation of postoperative imaging.

Toxicity and Aesthetic Outcome

The interaction between oncoplastic surgery and radiotherapy directly influences late cosmetic outcomes.

The main radiotherapy-related effects include:

- Fibrosis;
- Scar retraction;
- Edema;
- Pigmentary changes;
- Telangiectasias;
- Progressive asymmetry.

However, studies have demonstrated that immediate breast remodeling frequently reduces late deformities when compared with conventional breast-conserving surgery without reconstruction.

Adequate redistribution of breast tissue may minimize localized retractions induced by radiotherapy.

Importance of the Multidisciplinary Approach

The multidisciplinary approach represents one of the fundamental pillars of modern breast cancer treatment and plays an even more relevant role in oncoplastic surgery. The technical complexity of breast preservation combined with reconstructive remodeling requires continuous integration among different medical specialties, allowing individualized treatment planning, greater oncological safety, and better aesthetic and functional outcomes.

Oncoplastic surgery goes beyond the boundaries of traditional breast-conserving surgery by combining principles of breast surgery, plastic surgery, radiology, pathology, medical oncology, and radiation oncology. Thus, adequate treatment depends on effective communication among all professionals involved.

Several international consensus statements emphasize that multidisciplinary integration is associated with fewer treatment failures, better radiotherapy planning, a reduced need for reoperations, and greater patient satisfaction.^{6,7}

Integration Among Specialties

The appropriate management of oncoplastic breast-conserving surgery depends on coordinated collaboration among different specialists.

Breast Surgeon

The breast surgeon plays a central role in the oncological planning of surgery and is responsible for clinical assessment, defining tumor resection, disease staging, and choosing the breast-conserving strategy.

In addition, the breast surgeon should have knowledge of oncoplastic techniques in order to integrate oncological safety and aesthetic outcomes.

Radiation Oncologist

The radiation oncologist plays an essential role in planning adjuvant radiotherapy after oncoplastic surgery.

Glandular remodeling may make identification of the tumor bed more difficult, making communication regarding the following essential:

- Technique used;
- Tumor location;
- Resected volume;
- Clip placement;
- Glandular redistribution.

Adequate delineation of the tumor bed is essential for administration of the radiotherapy “boost.”

Radiologist

The radiologist participates in both the diagnostic phase and postoperative follow-up.

The radiologist's functions include:

- Preoperative localization of the lesion;
- Assessment of tumor extent;
- Identification of multifocality;
- Localization of non-palpable lesions;
- Interpretation of postoperative changes.

After oncoplastic surgery, imaging examinations become more complex due to the presence of fibrosis, fat necrosis, and architectural distortions.

Pathologist

The pathologist plays a critical role in the assessment of surgical margins and pathological evaluation of the surgical specimen.

Adequate anatomical orientation of the specimen is essential for:

- Identification of involved margins;
- Radiological correlation;
- Planning of possible reinterventions.

Medical Oncologist

The medical oncologist is involved in systemic treatment planning, including:

- Chemotherapy;
- Hormone therapy;
- Targeted therapies;
- Immunotherapy.

Tumor response to neoadjuvant treatment may significantly modify the surgical strategy and expand the possibilities of oncoplastic breast-conserving surgery.

Surgical Report

The operative report is of fundamental importance in oncoplastic surgery and should contain a detailed description of the technique employed.

The minimum recommended information includes:

- Oncoplastic technique used;
- Tumor location;
- Estimated resection volume;
- Anatomical orientation of the specimen;
- Clip placement;
- Type of glandular remodeling performed;
- Pedicle used;
- Contralateral symmetrization;
- Presence of flaps.

These data are essential for the radiation oncologist, radiologist, and follow-up team.

Preoperative and postoperative photographic documentation is also of increasing relevance for aesthetic assessment and longitudinal follow-up.

Complications

Complications of oncoplastic surgery can be divided into early and late complications. Although most procedures have a good safety profile, greater technical complexity may increase certain surgical risks compared with conventional breast-conserving surgery.

Complication rates vary according to:

- Technique used;
- Extent of resection;
- Breast volume;
- Comorbidities;
- Experience of the surgical team.

Early Complications

Early complications generally occur within the first few weeks after the procedure.

Seroma

Seroma is one of the most frequent complications, particularly after extensive glandular dissection and the use of flaps.

It may cause:

- Discomfort;

- Secondary infection;
- Delayed wound healing.

Hematoma

Hematoma may compromise flap vascularization and increase the risk of tissue necrosis. Large hematomas may require surgical reintervention.

Infection

Postoperative infection may compromise the aesthetic outcome and delay the initiation of adjuvant radiotherapy or chemotherapy.

Patients with obesity, diabetes, and those who smoke have a higher risk of infection.

Dehiscence

Wound dehiscence occurs mainly in areas of greater scar tension, particularly at “inverted-T” junctions.

Fat Necrosis

Fat necrosis results from vascular compromise of adipose tissue and may present as:

- Palpable nodules;
- Induration;
- Calcifications;
- Radiological changes.

It may mimic tumor recurrence on imaging examinations.

Nipple-Areola Complex (NAC) Necrosis

NAC necrosis represents one of the most feared complications of therapeutic mammoplasties. The main risk factors include:

- Smoking;
- Obesity;
- Long pedicles;
- Extensive resections;
- Diabetes.

Late Complications

Late complications are generally related to healing and the effects of radiotherapy.

Fibrosis

Fibrosis may cause breast induration and progressive retraction.

Asymmetry

Even after initial symmetrization, radiotherapy-induced changes may result in progressive asymmetry over time.

Scar Retraction

Scar retraction may significantly compromise breast contour and the position of the NAC.

Post-Radiotherapy Changes

Late effects of radiotherapy include:

- Edema;
- Fibrosis;
- Telangiectasias;
- Pigmentary changes;
- Tissue contraction.

Fat Necrosis

Late fat necrosis may present years after the procedure and is frequently mistaken for tumor recurrence.

Risk Factors for Complications

Several factors increase the incidence of complications in oncoplastic surgery.

Smoking

Smoking compromises microcirculation and increases the risk of:

- Necrosis;
- Infection;
- Dehiscence;
- Vascular compromise of the NAC.

Obesity

Patients with obesity have a higher risk of:

- Seroma;
- Infection;
- Fat necrosis;
- Anesthetic complications.

Diabetes

Diabetes is associated with impaired wound healing and a higher risk of infection.

Radiotherapy

Radiotherapy increases the risk of fibrosis, retraction, and late aesthetic changes.

Extensive Resections

Large resections increase tissue tension and the risk of deformities.

Aesthetic Outcomes and Quality of Life

Oncoplastic surgery has brought about an important change in the concept of therapeutic success in breast cancer. Currently, aesthetic and psychosocial outcomes are considered an integral part of oncological treatment.

Several studies using validated instruments, such as the BREAST-Q, demonstrate high levels of satisfaction after oncoplastic surgery.

Psychosocial Benefits

The main benefits include:

- Better body image;
- Greater patient satisfaction;
- Reduced psychological impact;
- Preservation of femininity;
- Better sexual quality of life;
- Better social reintegration.

Patients undergoing oncoplastic surgery frequently report a lower perception of bodily mutilation compared with mastectomy and conventional breast-conserving surgery.

Aesthetic Satisfaction

Immediate breast remodeling allows:

- Better symmetry;
- Preservation of breast contour;
- Reduction of deformities;
- Better positioning of the NAC.

Meta-analyses demonstrate high levels of aesthetic satisfaction and better quality of life compared with conventional breast-conserving surgery.

Future Perspectives

Oncoplastic surgery continues to evolve rapidly, keeping pace with technological advances and trends toward individualized treatment.

Image-Guided Surgery

The integration of intraoperative imaging and three-dimensional surgical planning is expected to increase the precision of resections.

Minimally Invasive Techniques

Endoscopic approaches and smaller incisions are being studied to reduce morbidity and improve aesthetic outcomes.

Biomaterials

The use of acellular dermal matrices and biomaterials may expand reconstructive options for complex defects.

Adjunctive Fat Grafting

Fat grafting has been widely used to correct irregularities, improve the quality of irradiated tissue, and provide aesthetic refinement.

Robotic Surgery

The application of robotic surgery in breast reconstruction is still in its early stages but has the potential to reduce scarring and morbidity.

Artificial Intelligence

Artificial intelligence may contribute in the future to:

- Objective assessment of symmetry;
- Surgical planning;
- Prediction of complications;
- Automated aesthetic analysis.

Surgical De-escalation

The contemporary trend in breast oncology prioritizes less invasive and more individualized treatments.

Increasing rates of pathological complete response after neoadjuvant therapies may directly influence the future of breast-conserving resections.

CONCLUSION

Oncoplastic surgery has revolutionized the breast-conserving treatment of breast cancer by allowing wider resections without significantly compromising aesthetic outcomes. The integration of oncological principles and reconstructive techniques has expanded the therapeutic possibilities of breast preservation, providing better psychosocial outcomes and high levels of patient satisfaction.

Current evidence demonstrates that oncoplastic surgery maintains high standards of oncological safety, with local recurrence and survival rates equivalent to those of conventional breast-conserving surgery, in addition to lower rates of deformity and reoperations.¹⁻⁵

Mastery of oncoplastic techniques has become an essential skill for the modern breast surgeon. However, the success of this approach depends directly on adequate preoperative planning, careful patient selection, and multidisciplinary integration among breast surgery, plastic surgery, radiology, pathology, medical oncology, and radiation oncology.

Thus, oncoplastic surgery has become established as one of the fundamental pillars of contemporary breast cancer treatment, representing an important advance in the pursuit of increasingly effective, individualized therapies centered on the patient's quality of life.¹⁰⁻¹⁶

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RISK FACTORS, DIAGNOSIS, AND CLINICAL OUTCOMES IN ABDOMINAL AORTIC ANEURYSM: AN INTEGRATIVE LITERATURE REVIEW

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ABSTRACT

Introduction: abdominal aortic aneurysm (AAA) is a multifactorial and often asymptomatic condition characterized by progressive and irreversible dilation of the aortic wall, with a high risk of rupture and sudden death. It is more prevalent in men over 65 years, especially smokers, and is usually diagnosed incidentally. **OBJECTIVES:** To synthesize scientific evidence on risk factors, diagnostic methods, and clinical outcomes related to AAA through an integrative literature review. **Methodology:** This is an integrative literature review with searches conducted in PubMed from 01/01/2020 to 06/30/2025, using MeSH/DeCS descriptors combined with Boolean operators. Eligible studies included observational studies, case series with $n \geq 50$, clinical trials and systematic reviews with quantitative data. **Results and discussion:** AAA was associated with male sex, advanced age, smoking, hypertension, dyslipidemia, and family history. Ultrasound is the preferred screening method, while computed tomography is essential for surgical planning. Early intervention, preferably with endovascular repair (EVAR), reduces mortality, though it requires ongoing monitoring. Open surgery remains a valid option in selected cases. Controlling risk factors is crucial to prevent complications. **Conclusion:** Screening high-risk groups, early diagnosis, and appropriate surgical intervention are essential to reduce AAA-related mortality.

Keywords: Abdominal aortic aneurysm, Risk factors, Diagnosis, Clinical outcomes, Endovascular repair.

INTRODUCTION

Aortic aneurysm is a pathological condition characterized by a progressive and irreversible dilation of the aortic wall. The most common type is the abdominal aortic aneurysm (AAA), which is defined when the diameter of the affected segment reaches 3.0 cm or more, often representing an increase of more than 50% compared with the normal diameter of the vessel lumen. The main pathophysiological mechanisms involved include protein destabilization of the extracellular matrix, endothelial dysfunction, and chronic inflammation of the aortic wall, leading to the loss of vascular elasticity.¹

Clinically, the progression of most cases of AAA is asymptomatic until rupture occurs. For this reason, the identification of risk factors is essential for the screening and clinical management of the disease. Among the main associated variables, the following stand out: male sex, advanced

age, smoking, family history of AAA, systemic arterial hypertension, dyslipidemia, coronary artery disease, and peripheral arterial disease.^{2,3}

The diagnosis of AAA, given its silent nature, is often made incidentally during imaging examinations requested for other purposes. However, symptoms such as unexplained abdominal discomfort associated with low back pain, a palpable pulsatile mass, and hypotension may be suggestive of aneurysmal rupture, which requires immediate evaluation. Abdominal ultrasonography is the method of choice for investigation in at-risk individuals, as it has high sensitivity, is non-invasive, and is low cost.^{4,3}

The main clinical outcomes of abdominal aortic aneurysm (AAA) include rupture, sudden death, the need for emergency surgical intervention, and postoperative complications. Rupture is the most critical outcome, with a mortality rate of over 80% in cases without hospital care and up to 50% even with immediate medical assistance. Sudden death, related to late-diagnosed rupture, is more common in individuals with large aortic protrusions (>5.5 cm) or with rapid aneurysm growth.^{5,3,1} When identified early, AAA can be treated electively, usually through endovascular aneurysm repair (EVAR), a technique that reduces immediate morbidity and mortality. Postoperative complications include the occurrence of endoleaks, graft thrombosis, and endograft migration.^{6,7}

OBJECTIVE

This study aims to synthesize, through an integrative review, the evidence available in the scientific literature regarding the risk factors, diagnostic methods, and clinical outcomes associated with abdominal aortic aneurysm.

METHODOLOGY

This This is an integrative literature review, aimed at synthesizing scientific evidence on risk factors, diagnostic methods, and clinical outcomes related to abdominal aortic aneurysm (aortic aneurysm, abdominal), as indexed in the controlled vocabularies MeSH (Medical Subject Headings) and DeCS (Health Sciences Descriptors). Studies published between January 1, 2020, and June 30, 2025, in Portuguese and English, were included.

Eligibility Criteria and Study Selection

Eligible studies included: observational studies (cohort and case-control), case series with $n \geq 50$, randomized or non-randomized clinical trials, and systematic reviews with quantitative data.

The following were excluded: isolated case reports, narrative reviews, expert opinions not based on primary data, and letters to the editor.

Search Strategy: the search was conducted in the PubMed database, using combinations of MeSH/DeCS descriptors with Boolean operators, according to the objectives of the review. Below is an example of the strategy applied in the PubMed database: ("Aortic Aneurysm, Abdominal"[MeSH] OR "Aneurisma da aorta abdominal"[DeCS]) AND ("Risk Factors"[MeSH] OR "Fatores de risco"[DeCS]) AND ("Diagnosis"[MeSH] OR "Diagnóstico"[DeCS]) AND ("Treatment"[MeSH] OR "Terapêutica"[DeCS]) AND ("2020/01/01"[Date - Publication] : "2025/06/30"[Date - Publication])

Study Selection and Data Extraction Process

Screening was carried out in two stages by independent reviewers: (1) title and abstract screening and (2) full-text review. Any disagreements were resolved by consensus. The extracted

data included: methodological characteristics of the study, population, interventions or exposures, analyzed outcomes, main findings, and limitations reported by the authors.

RESULTS AND DISCUSSION

Abdominal aortic aneurysm (AAA) is a frequently asymptomatic condition, often being detected incidentally during imaging examinations requested for other reasons.^{5,4,2} Despite its silent nature, the aneurysm is potentially lethal in the event of rupture - an event associated with high mortality rates, being responsible for approximately 170,000 deaths annually worldwide.^{4,1,7}

The prevalence of AAA is related to demographic, behavioral, and genetic factors. Male sex, advanced age, and smoking stand out. It is more common in men, and its incidence increases significantly after 65 years of age.⁴ In women, although less prevalent, AAA tends to grow more rapidly and rupture at smaller diameters, from 4.5 cm onward.^{7,4} Smoking is the main modifiable risk factor, increasing incidence, accelerating aneurysm growth, and increasing the risk of rupture—its cessation being recommended with Class I level of evidence.^{4,7,1} In addition, arterial hypertension, coronary artery disease, and peripheral arterial disease are frequently associated comorbidities and act as independent risk factors for the development of AAA.^{4,7,2} Dyslipidemia - that is, elevated levels of LDL cholesterol and lipoprotein(a) - has a potentially causal role, and the use of statins may attenuate aneurysm growth.^{7,4} Obesity, on the other hand, may be associated with slower AAA growth.⁷ Chronic inflammatory diseases also contribute to its pathogenesis.^{4,1,8} Furthermore, family history of AAA has a strong genetic component, with heritability reaching up to 70%, and the risk of development and rupture in first-degree relatives being substantially higher—by about 10 times.^{4,7,1} Although physical inactivity and alcohol consumption are considered additional factors, the evidence regarding their association is still limited.⁴

The pathophysiology of AAA involves destruction of the extracellular matrix (ECM), chronic inflammation, and apoptosis of smooth muscle cells (SMCs).^{4,7} The degradation of the ECM, including elastin and collagen, is mediated by matrix metalloproteinases (MMPs) released by inflammatory cells such as neutrophils and macrophages,⁴ weakening the aortic wall and predisposing it to progressive dilation and, eventually, rupture.^{4,7} Endothelial dysfunction is an early pathological event that contributes to oxidative stress and inflammation in the arterial wall.¹ Chronic inflammation also includes the transdifferentiation of SMCs into macrophage-like cells.⁴ Studies of flow-mediated dilation (FMD) inversely correlate endothelial dysfunction with aneurysm diameter, with smoking contributing to this dysfunction.¹ DNA demethylation and oxidative stress also modulate gene expression and apoptosis of SMCs, increasing susceptibility to dilation and rupture.⁴

With regard to diagnosis, it is known that it is frequently incidental, being detected in imaging examinations for other clinical reasons, since it is generally asymptomatic until rupture.^{3,5,4} Abdominal ultrasonography is the examination of choice for screening, and it is recommended for men aged 65 to 75 years who are smokers or former smokers.^{3,4} Its choice is due to being cost-effective, non-invasive, and radiation-free, in addition to having high sensitivity (94–100%) and specificity (98–100%) in the detection of AAA.³ It is also used for the initial diagnosis and periodic monitoring of small aneurysms.^{5,4} Accuracy, however, may be limited by obesity or intestinal gas.^{3,4} Computed tomography (CT) is the gold standard for diagnostic confirmation and surgical planning, providing detailed assessment of diameter, extension, and wall characteristics, in addition to mapping the aorta and adjacent arteries.⁴ It is crucial for cases that require intervention, such as aneurysms larger than 5.5 cm in men or 5.0 cm in women,

or with rapid growth (>0.5 cm in 6 months or >1 cm in 1 year).^{3,4} For greater precision, measurements should be taken from the outer edge of the vessel wall, in the true axial direction of the aorta, using multiplanar and three-dimensional reconstructions.⁴ Magnetic resonance imaging (MRI), although less common and with limitations such as availability, claustrophobia, and presence of metallic devices, may be an option in specific cases, mainly because it does not require the use of iodinated contrast or radiation. Regardless of the imaging method, regular surveillance is essential to monitor aneurysm growth and determine the appropriate moment for intervention.^{4,3}

According to clinical guidelines, AAA follow-up depends on the initial diameter.^{4,2} Aneurysms below 3.0 cm do not require regular follow-up.⁴ Those between 3.0 and 5.4 cm should be monitored every 6 to 12 months, depending on the growth rate.⁴ Surgical intervention is generally indicated upon reaching 5.5 cm in men or 5.0 cm in women,² in cases of accelerated growth (>0.5 cm in 6 months or >1 cm in 1 year), or presence of symptoms.^{7,4,2}

With regard to clinical outcomes, the prognosis of the aneurysm is intrinsically linked to its early diagnosis and adequate treatment.^{5,4} AAA rupture is a serious medical emergency, frequently lethal in most cases when untreated.⁴ Historically, in-hospital mortality for ruptured aneurysm reached 50%,⁴ but the dissemination of endovascular treatment has led to a reduction to the 20% to 30% range.⁴ In contrast, elective intervention, performed before rupture, is associated with significantly lower rates of mortality and complications.^{5,4}

The two main surgical approaches for the treatment of abdominal aortic aneurysm are conventional open surgery and endovascular repair (EVAR).^{6,4} EVAR has gained prominence in recent decades for being a less invasive procedure and has been the most common surgical approach for AAA due to patient preference.^{6,4} When compared with open surgery, EVAR generally promotes faster recovery, presents lower rates of perioperative complications, and lower 30-day mortality.^{6,4} In addition, patients undergoing EVAR typically have shorter surgical time, lower blood loss, shorter hospital stay, and shorter stay in intensive care units, with fewer immediate postoperative cardiac and respiratory complications.⁴ However, EVAR requires continuous and rigorous follow-up with imaging examinations, such as annual CT angiographies.^{6,4} This is due to the significantly higher risk of complications and need for reintervention over time, with endoleaks, endograft migration, and material failures being the most frequent.^{6,4} Although mortality is lower, the rates of reinterventions and adverse events are generally more frequent in EVAR than in open surgery.⁴

On the other hand, open surgery remains an essential option, especially for patients with anatomy unfavorable to EVAR.^{6,4} Although it may have greater perioperative morbidity and be less suitable for patients with severe comorbidities or advanced age, open surgery demonstrates excellent long-term results and lower need for reoperations compared with EVAR.^{6,4} After open surgery, imaging follow-up is less intense, with CT of the aorta and iliac arteries being recommended every 5 years.⁴

In the management of AAA, preventive strategies and health education are crucial.⁵ Targeted screening campaigns are fundamental for early detection.⁴ In addition, strict control of risk factors, such as smoking and hypertension, is essential to reduce progression and avoid adverse outcomes.^{4,7} Finally, postoperative surveillance is vital to detect complications early, such as endoleaks or recurrence of aortic dilation.^{6,4} The frequency of imaging examinations depends on the intervention: CT angiography is recommended 30 days after endovascular repair (EVAR) and annually thereafter, or every 5 years after open repair.⁴

CONCLUSION

Finally, the present study states that abdominal aortic aneurysm (AAA) is a pathological condition associated with several factors, generally asymptomatic, and presents a high risk of death, especially in cases of rupture. Therefore, early diagnosis is essential to reduce mortality related to AAA, demonstrating the essentiality of screening in risk groups, such as male smokers aged 65 to 75 years and patients with a family history of aneurysm. However, screening is not sufficient to prevent aneurysmal rupture; lifestyle changes are also crucial to control disease progression, such as blood pressure control and smoking cessation. Although surgical techniques, such as open surgery and endovascular repair (EVAR), provide immediate benefits, especially when performed before vessel rupture, post-surgical follow-up is indispensable, since it allows anticipation of management in the face of possible complications.

It is therefore concluded that, although AAA, in most cases, does not present symptoms, its control and treatment are possible through early screening, identification, and intervention based on the most affected groups. It is also important to seek the improvement and innovation of the surgical procedures used for intervention in cases of abdominal aortic aneurysm, with the aim of reducing the deaths caused by this condition.

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FACTORS INFLUENCING POSTOPERATIVE INFECTION IN ARTHROPLASTIES

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ABSTRACT

Introduction: Periprosthetic infection (PI) is one of the most severe complications of total arthroplasty, with significant impact on morbidity, mortality, and healthcare costs. **Objective:** To synthesize the available evidence on factors that influence the development of postoperative infections in arthroplasty, providing evidence-based recommendations for clinical practice. **Methods:** A systematic search was conducted in the PubMed, Web of Science, and Scopus databases for studies published between 2006 and 2023 on periprosthetic infection in total arthroplasty. Observational studies, clinical trials, and meta-analyses evaluating risk factors for periprosthetic infection in total hip arthroplasty (THA) and total knee arthroplasty (TKA) were included. **Results:** Nine studies were included, totaling approximately 1,200,000 patients. The identified risk factors were classified into: (1) patient-related factors (comorbidities, nutritional status, smoking); (2) surgical factors (surgery duration, procedure type); and (3) hospital and socioeconomic factors. The risk factors most consistently associated with periprosthetic infection were diabetes mellitus (OR = 3.72), obesity (OR = 2.53–4.00), rheumatologic disease (RR = 1.71), smoking (RR = 2.37), prolonged surgical duration, and congestive heart failure. **Conclusion:** Multiple factors influence the development of postoperative infections in total arthroplasty. Identifying and optimizing these modifiable risk factors is essential to reduce the incidence of periprosthetic infection and improve clinical outcomes.

Keywords: Periprosthetic, Infection, Total arthroplasty, Risk factors, Surgical site infection.

INTRODUCTION

Arthroplasty is one of the most commonly performed surgical procedures worldwide, with more than two million procedures carried out annually.¹ Despite significant advances in surgical techniques, implant materials, and infection prevention protocols, periprosthetic infection (PPI) remains a devastating complication, adversely affecting patients' quality of life and generating substantial costs for healthcare systems.²

Periprosthetic infection is defined as the presence of viable microorganisms in periprosthetic tissue, confirmed by microbiological culture or histopathological findings.³ This complication may occur at any time after arthroplasty and is commonly classified as early infection (up to 3 months), delayed infection (3–24 months), or late infection (>24 months).⁴

The incidence of periprosthetic infection varies considerably across studies, depending on the population analyzed, the type of arthroplasty (primary versus revision), the anatomical site involved (hip versus knee), and the duration of follow-up.⁵ Recent studies suggest that the incidence of periprosthetic infection after primary total arthroplasty ranges from 0.3% to 2%, whereas in revision arthroplasty it may reach up to 10%.⁶

Risk factors for periprosthetic infection are multiple and complex and can be classified into three main categories: (1) patient-related factors (age, sex, comorbidities, nutritional status, smoking); (2) surgery-related factors (type of procedure, duration, and surgical technique); and (3) hospital-related and socioeconomic factors.⁷ Identification of these risk factors is essential for preoperative risk stratification and for the implementation of targeted preventive strategies.⁸

The economic impact of periprosthetic infection is substantial. Recent studies indicate that the incremental costs associated with periprosthetic infection may range from US\$ 20,000 to US\$ 80,000 per patient, depending on infection severity and the need for revision procedures.⁹

Therefore, this systematic review was conducted with the aim of synthesizing the available evidence on factors influencing the development of postoperative infections in arthroplasty, providing evidence-based recommendations to support clinical practice.

METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁰ A systematic search was performed in the PubMed, Web of Science, and Scopus databases on [date], using the following search terms: ("periprosthetic infection" OR "prosthetic joint infection" OR "surgical site infection" OR "deep surgical site infection") AND ("total hip arthroplasty" OR "total knee arthroplasty" OR "hip replacement" OR "knee replacement") AND ("risk factors" OR "incidence" OR "epidemiology"). The search was limited to articles published in English between January 2006 and December 2023. Reference lists of included studies were also screened to identify additional relevant publications.

Observational studies (prospective and retrospective cohort studies, cross-sectional studies), clinical trials, and meta-analyses evaluating risk factors or incidence of periprosthetic infection in total arthroplasty were included. Studies involving adult patients (≥ 18 years) undergoing primary or revision total hip or knee arthroplasty were eligible, with no restrictions regarding sex, race, or ethnicity. The primary outcomes were: (1) risk factors associated with periprosthetic infection; and (2) incidence of periprosthetic infection.

The exclusion criteria were: (1) studies published in languages other than English; (2) studies including fewer than 100 patients; (3) narrative reviews, editorials, and commentaries; (4) studies focused exclusively on infection prevention without reporting incidence data or risk factors; and (5) studies with follow-up shorter than six months.

Study selection and data extraction were independently performed by two reviewers using a standardized data extraction form. Extracted data included study characteristics (author, year, country, study design), population characteristics (number of patients, mean age, sex, type of arthroplasty), outcomes (infection incidence, risk factors), and methodological aspects (duration of follow-up, infection definition, statistical methods). Disagreements were resolved by consensus or consultation with a third reviewer. Studies were classified as having low, moderate, or high risk of bias.

RESULTS

The systematic search identified 1,232 studies. After application of the inclusion and exclusion criteria, 85 studies remained for full-text evaluation, of which 9 studies were ultimately included in the qualitative analysis (Figure 1). The 9 included studies were published between 2006 and 2023 and comprised a total sample of approximately 1,200,000 patients. Quality assessment of the included studies using appropriate appraisal tools indicated that 7 of the 9 studies were classified as high quality, while 2 studies were classified as moderate quality. No studies were classified as low quality.

Table 1: Characteristics of the 9 Studies Included in the Systematic Review

Study	Year	Country	Study design	N	Type of arthroplasty	Follow-up	Quality
Edmiston et al. ¹¹	2023	USA	Retrospective cohort	20.468	Primary and revision THA	12 months	High
Tella et al. ¹²	2022	Italy	Prospective cohort	583	Primary THA	596 days	High
Bozic et al. ¹³ (ATQ)	2012	USA	Retrospective cohort	40.919	Primary THA	90 days	High
McMaster ¹⁴ MAC	2022	Canada	Retrospective cohort	129.613	Primary TKA	15 years	High
Ko et al. ¹⁵	2021	South Korea	Retrospective cohort	560.954	Primary and revision TKA	Variable	Moderate
Bozic et al. ¹⁶ (ATJ)	2012	USA	Retrospective cohort	83.011	Primary TKA	90 days	High
Kurtz et al. ¹⁷	2010	USA	Retrospective cohort	69.663	Primary TKA	10 years	High
Chen et al. ¹⁸	2013	China	Meta-analysis	57.223	Primary TKA	Variable	Moderate
Singh et al. ¹⁹	2015	USA	Prospective cohort	7.926	Primary THA and TKA	Variable	High

THA = Total Hip Arthroplasty; TKA = Total Knee Arthroplasty; N = Number of patients.

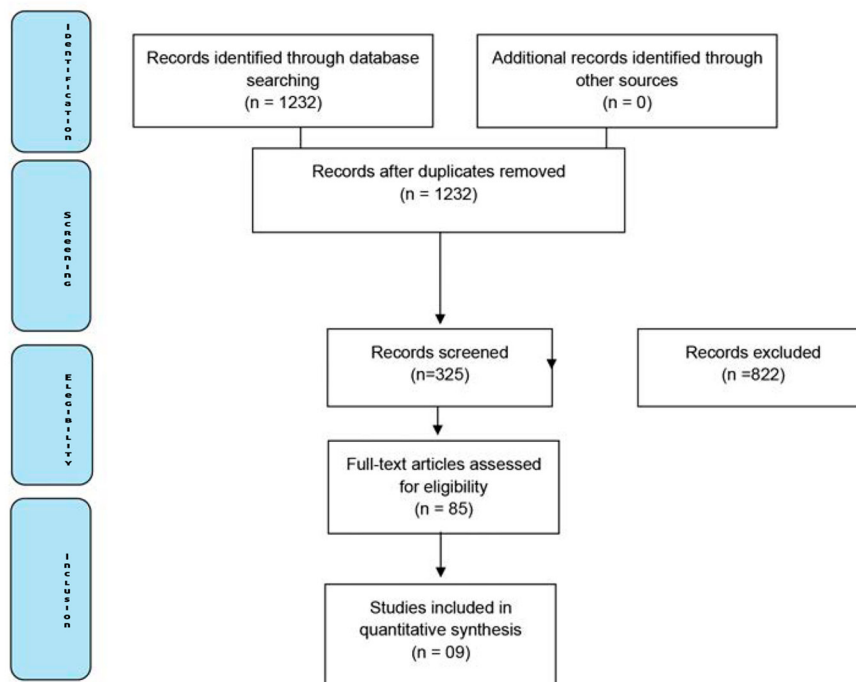


Figure 1: Flowchart of articles.

Table 2: Risk Factors for Periprosthetic Infection Identified in the Included Studies

Risk factor	Effect measure	Confidence interval	Type of arthroplasty	Study
Diabetes Mellitus	OR = 3,72	2.30-6.01	TKA	Chen et al.
Obesity (BMI > 40)	OR = 4,00	1.23-12.98	TKA	Chen et al.
Obesity (BMI > 30)	OR = 2,53	1.25-5.13	TKA	Chen et al.
Rheumatologic disease	RR = 1,71	-	THA	Bozic et al.
Rheumatoid arthritis	OR = 1,83	1.42-2.36	TKA	Chen et al.
Heart failure	Independent risk factor	-	TKA	Bozic et al.
Chronic pulmonary disease	Independent risk factor	-	TKA	Bozic et al.
Preoperative anemia	RR = 1,36	-	THA	Bozic et al.
Smoking (deep infection)	RR = 2,37	1.19-4.72	THA/TKA	Singh et al.
Smoking (implant revision)	RR = 1,78	1.01-3.13	THA/TKA	Singh et al.
Male sex	Risk factor	-	TKA	Ko et al.
Household income	Risk factor	-	TKA	Ko et al.
Length of hospital stay ≥ 35 days	Risk factor	-	TKA	Ko et al.
Blood transfusion requirement	Risk factor	-	TKA	Ko et al.

THA = Total Hip Arthroplasty; TKA = Total Knee Arthroplasty; OR = Odds Ratio; RR = Risk Ratio; BMI = Body Mass Index.

Table 3: Incidence of Periprosthetic Infection by Type of Arthroplasty

Type of arthroplasty	Subtype	Incidence	Study
THA	Primary – Superficial infection	0.67% (IC 95% 0,55%-0,79%)	Edmiston et al.
THA	Primary – Deep infection	0.30% (IC 95% 0,22%-0,39%)	Edmiston et al.
THA	Revision – Superficial infection	4.8% (IC 95% 4,0%-5,6%)	Edmiston et al.
THA	Revision – Deep infection	8.9% (IC 95% 7,8%-10,0%)	Edmiston et al.
TKA	Primary - 1 year	0.51%	McMaster MAC
TKA	Primary - 5 years	1.12%	McMaster MAC
TKA	Primary - 10 years	1.49%	McMaster MAC
TKA	Primary - 15 years	1.65%	McMaster MAC
TKA	Primary - 2 years	1.55%	Kurtz et al.
TKA	Primary - 2-10 years	0.46%	Kurtz et al.

THA = Total Hip Arthroplasty; TKA = Total Knee Arthroplasty; CI = Confidence Interval.

DISCUSSION

The results demonstrate that periprosthetic infection is a multifactorial complication in which multiple patient-related, surgical, and socioeconomic factors interact to determine the overall risk of infection. This systematic review synthesized the available evidence on factors influencing the development of postoperative infections in total arthroplasty, revealing important insights into the complexity and multiplicity of the associated risk factors.

The findings of this review confirm that comorbidities are major risk factors for periprosthetic infection.¹⁸ Diabetes mellitus was identified as one of the most significant risk factors, with an odds ratio of 3.72 in a meta-analysis of 12 studies,¹⁸ indicating that diabetic patients have approximately a 3.7-fold higher risk of developing periprosthetic infection compared with non-diabetic individuals. This finding is consistent with the literature demonstrating that hyperglycemia impairs immune response through multiple mechanisms, including neutrophil dysfunction, impaired chemotaxis, and reduced bactericidal activity,²⁰ in addition to compromising wound healing via adverse effects on angiogenesis and collagen synthesis.²¹⁻²³ The clinical relevance of this finding is substantial, suggesting that optimization of perioperative glycemic control in diabetic patients may be an effective strategy for reducing periprosthetic infections.²¹

Rheumatologic disease was identified as a significant risk factor in multiple studies, with a reported risk ratio of 1.71 in a cohort of 40,919 patients,¹³ while a meta-analysis found an odds ratio of 1.83 specifically for rheumatoid arthritis.¹⁸ This association may be attributed to the immunosuppressive effects of both the underlying rheumatologic condition and the medications used in its treatment, particularly biologic agents and corticosteroids. In addition, patients with rheumatologic diseases frequently present with other comorbidities that further increase infection risk, creating a cumulative risk effect.²² Congestive heart failure was also identified as an independent risk factor for periprosthetic infection,¹⁶ likely due to impaired tissue perfusion and compromised immune response. Reduced cardiac output and venous congestion result in tissue hypoxia, which negatively affects wound healing and diminishes the ability of immune cells to combat infection.²³

Nutritional and metabolic factors also played an important role in the findings of this review. Obesity was identified as a significant risk factor for infection, with odds ratios ranging from 2.53 for body mass index (BMI) $>30 \text{ kg/m}^2$ to 4.00 for BMI $>40 \text{ kg/m}^2$,¹⁸ indicating a progressive increase in risk with greater degrees of obesity. The literature further demonstrates that obesity impairs tissue perfusion, prolongs surgical duration, and compromises immune response through multiple mechanisms, including chronic inflammation, T-cell dysfunction, and reduced opsonization.²⁴ In addition, obese patients often experience longer operative times, increased blood loss, and a greater need for blood transfusion, all of which contribute to an elevated risk of infection.²⁴

Preoperative anemia was identified as a significant risk factor, with a reported risk ratio of 1.36,¹³ a finding consistent with the pathophysiological role of anemia in reducing oxygen delivery to tissues—an essential factor for wound healing and effective immune response. Tissue hypoxia resulting from anemia impairs neutrophil bactericidal activity and reduces collagen synthesis, thereby compromising surgical wound integrity.²⁵

Smoking was identified as a significant risk factor for deep infection, with a risk ratio of 2.37, and for implant revision, with a risk ratio of 1.78,¹⁹ findings that align with extensive literature demonstrating the deleterious effects of smoking on wound healing.²⁶ Tobacco use induces vasoconstriction and reduces tissue perfusion, impairs neutrophil and macrophage function, decreases collagen synthesis, and promotes a proinflammatory state.²⁶ Moreover, smokers frequently present with additional comorbidities, such as chronic pulmonary disease, which further increase the risk of postoperative complications.¹⁹ These findings have important clinical implications, suggesting that smoking cessation prior to elective surgery may be an effective strategy for reducing periprosthetic infections.²⁶

Prolonged surgical duration was also identified as a risk factor for infection,¹⁹ with infected patients exhibiting a mean operative time of 127 minutes compared with 94 minutes in non-infected patients—a difference of 33 minutes. This finding is consistent with evidence demonstrating that longer surgical duration increases the risk of intraoperative contamination due to prolonged wound exposure, greater risk of hypothermia, and potential inadequacy of antibiotic prophylaxis.⁹ Furthermore, prolonged operative time often reflects greater surgical complexity or technical difficulty, both of which are associated with increased tissue trauma and heightened inflammatory response.⁹ Notably, surgical duration showed positive correlations with patient weight, BMI, and number of comorbidities,¹⁹ suggesting that high-risk patients are more likely to undergo prolonged procedures, thereby creating a cumulative risk effect.

Demographic and socioeconomic factors also influenced the development of infection.¹⁵ Male sex was identified as a risk factor in multiple studies,¹⁵ a finding that may reflect differences in postoperative activity patterns, adherence to weight-bearing restrictions, and general risk-related behaviors.⁸ Household income and length of hospital stay were identified as socioeconomic factors associated with increased infection risk,¹⁵ potentially reflecting disparities in access to high-quality postoperative care, adherence to follow-up, and opportunities for preoperative optimization.⁷ These findings suggest that socioeconomic inequities may significantly influence total arthroplasty outcomes, representing an important public health and health equity concern.⁷

The findings of this review carry several important clinical implications for orthopedic practice. First, routine preoperative risk stratification should be implemented, with patients presenting multiple risk factors undergoing rigorous preoperative evaluation and optimization of comorbidities.

Diabetic patients should receive optimized perioperative glycemic control, with maintenance of blood glucose levels between 140 and 180 mg/dL during the perioperative period.²¹ Obese patients should be counseled regarding preoperative weight loss, with studies suggesting that a 5–10% reduction in body weight may significantly reduce the risk of complications.⁷ Smokers should be advised to cease smoking at least four weeks prior to surgery, as this period is necessary for partial reversal of tobacco-related impairment in wound healing.²⁶ Patients with anemia should receive iron supplementation or preoperative transfusion as indicated, with maintenance of hemoglobin levels above 10 g/dL.²⁵ Patients with rheumatologic diseases should have their immunosuppressive regimens optimized in consultation with rheumatology specialists, with consideration of adjustments to antibiotic prophylaxis.²²

Minimization of surgical duration through efficient surgical techniques and surgeon experience is essential, as studies suggest that high-volume surgeons demonstrate lower infection rates.⁹ Consideration of minimally invasive techniques in high-risk patients may reduce tissue trauma and inflammatory response.⁹ Appropriate antibiotic prophylaxis, including redosing during prolonged procedures, is critical. Enhanced postoperative surveillance should be implemented in high-risk patients, with careful monitoring for early signs of infection and patient education regarding warning symptoms. Detailed preoperative counseling should be provided to patients with identified risk factors, informing them of the increased risk of periprosthetic infection and emphasizing the importance of adherence to activity restrictions and postoperative follow-up.²¹

CONCLUSION

This systematic review identified multiple factors that influence the development of postoperative infections in arthroplasty. The most significant risk factors included diabetes mellitus (OR = 3.72), obesity (OR = 2.53–4.00), rheumatologic disease (RR = 1.71), smoking (RR = 2.37), prolonged surgical duration, congestive heart failure, and preoperative anemia.

Identification and optimization of these modifiable risk factors are essential to reduce infection incidence and improve clinical outcomes. Targeted preventive strategies—including glycemic control, weight reduction, smoking cessation, and optimization of comorbid conditions—should be implemented in high-risk patients.

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IMPORTANCE OF NUTRITIONAL SUPPORT IN THE PRE- AND POSTOPERATIVE PERIODS OF ORTHOPEDIC SURGERY

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ABSTRACT

Total hip and knee arthroplasty are among the most frequently performed orthopedic procedures worldwide, with projections indicating exponential growth over the coming decades. Although long-term functional outcomes are favorable, the perioperative period is marked by a systemic inflammatory response, protein catabolism, and muscle atrophy—particularly of the quadriceps—that may impair recovery. Perioperative nutritional optimization has emerged as a promising strategy to mitigate surgical stress and enhance rehabilitation. Specific interventions, including essential amino acid supplementation, preoperative carbohydrate loading, and immunonutrition, have shown potential to preserve muscle mass, modulate metabolic response, and reduce postoperative complications. However, the literature remains fragmented, with significant methodological heterogeneity regarding populations, supplementation protocols, and outcome measures, underscoring the need for standardized clinical trials. Current evidence indicates that perioperative nutritional interventions are safe and effective in improving functional and metabolic outcomes after hip and knee arthroplasty. Personalized nutritional strategies tailored to patient characteristics represent a valuable opportunity to establish nutritional support as a standard component of perioperative orthopedic care.

Keywords: Arthroplasty, Perioperative nutrition, Essential amino acids, Immunonutrition, Functional recovery.

INTRODUCTION

Total hip and knee arthroplasty represent some of the most commonly performed orthopedic surgical interventions worldwide, with projections indicating exponential growth in the number of procedures over the coming decades. In the United States, Medicare data demonstrate that the annual volume of primary hip arthroplasty increased from 305,082 in 2013 to 594,981 in 2022, with projections reaching 2,174,382 procedures by 2040. For knee arthroplasty, projections are equally remarkable, with estimated increases of 139% by 2040 and 469% by 2060 compared with 2019 figures.^{1,2}

This exponential growth is driven by global population aging and the increasing prevalence of osteoarthritis, which affects approximately 365 million people worldwide, with 73% of cases occurring in individuals over 55 years of age.³

Although these procedures demonstrate excellent long-term functional outcomes, the perioperative period is characterized by a significant systemic inflammatory response, protein catabolism, and muscle atrophy that may compromise functional recovery. Quadriceps muscle strength loss may reach up to 62% in the immediate postoperative period, with a 10% reduction in muscle cross-sectional area, and this atrophy is particularly problematic in vulnerable populations such as older adults, individuals with diabetes, and patients with preexisting sarcopenia.⁴

Perioperative nutritional optimization has emerged as a promising strategy to mitigate the deleterious effects of surgical trauma and accelerate functional recovery. Specific nutritional interventions, including essential amino acid supplementation, preoperative carbohydrate loading, immunonutrition, and multimodal protocols, have demonstrated potential to preserve muscle mass, modulate the metabolic response, and reduce postoperative complications.⁵

Despite the growing interest in these interventions and evidence supporting their benefits, the literature remains fragmented, with studies showing significant methodological heterogeneity regarding populations, supplementation protocols, and assessed outcomes, thereby justifying the need for a systematic synthesis of the literature to guide evidence-based clinical practice.

Therefore, the aim of this study is to evaluate, through a literature review, the impacts of nutritional support in the preoperative and postoperative periods of orthopedic surgery.

METHODS

A literature review was conducted focusing on the identification of clinical trials and systematic reviews addressing the impact of nutritional support in patients undergoing orthopedic surgery, both in the preoperative and postoperative periods. The objective of the search was to gather and analyze recent scientific evidence investigating the influence of nutritional interventions on functional recovery, reduction of complications, and improvement of clinical outcomes in these patients.

The search was performed in the following electronic databases: PubMed/MEDLINE (via the National Library of Medicine), Scopus (Elsevier), Web of Science (Clarivate Analytics), SciELO (Scientific Electronic Library Online), and the Cochrane Library. These platforms were selected because of their broad coverage and relevance in indexing clinical studies and systematic reviews in the health sciences.

The search period included publications from January 2016 to October 2025. The selection of this timeframe aimed to ensure the inclusion of recent studies. The following inclusion criteria were established: randomized and non-randomized clinical trials; studies involving adult patients undergoing orthopedic surgery; investigations evaluating nutritional interventions, such as oral supplementation, specialized diets, enteral nutrition, or parenteral nutrition; and studies reporting outcomes related to functional recovery, length of hospital stay, wound healing, infection, or postoperative complications.

Exclusion criteria comprised observational studies without nutritional intervention, narrative reviews, case reports, editorials, experimental animal studies, and studies involving pediatric populations. Studies whose full text was not available in English, Spanish, or Portuguese were also excluded.

The article selection process was carried out in four main stages. Initially, titles and abstracts were screened to eliminate duplicates and studies unrelated to the topic. Subsequently, the full texts of potentially eligible articles were reviewed. A systematic extraction of data from the included studies was then performed, encompassing information regarding authors, year of publication, type of nutritional intervention, sample size, evaluated outcomes, and principal findings. Finally, a qualitative synthesis of the findings was conducted, allowing the identification of patterns and gaps in the available evidence.

The classification of levels of evidence and methodological strength proposed by the Oxford Centre for Evidence-Based Medicine (CEBM, 2011) was adopted. According to this classification, level 1A–1B studies correspond to high-quality randomized clinical trials or meta-analyses; levels 2A–2B include lower-quality controlled studies or cohort studies; level 3 encompasses case-control studies; and levels 4–5 refer to case series and expert opinions. Combinations of controlled descriptors and free-text keywords, in English and Portuguese, were used according to the Medical Subject Headings (MeSH) and Health Sciences Descriptors (DeCS) systems.

The primary search strategy, adapted for each database, was as follows:

("Nutritional Support" OR "Nutrition Therapy" OR "Perioperative Nutrition" OR "Dietary Supplementation")
AND ("Surgery" OR "Orthopedic Surgery")
AND ("Preoperative Period" OR "Postoperative Period")
AND ("Clinical Trial" OR "Randomized Controlled Trial")

Portuguese version (of SciELO and LILACS):

("Suporte Nutricional" OR "Terapia Nutricional" OR "Suplementação Dietética")
AND ("Cirurgia" OR "Cirurgia Ortopédica")
AND ("Período Pré-operatório" OR "Período Pós-operatório")

After applying the inclusion and exclusion criteria to each study, the relevant data were extracted and compiled in Table 1.

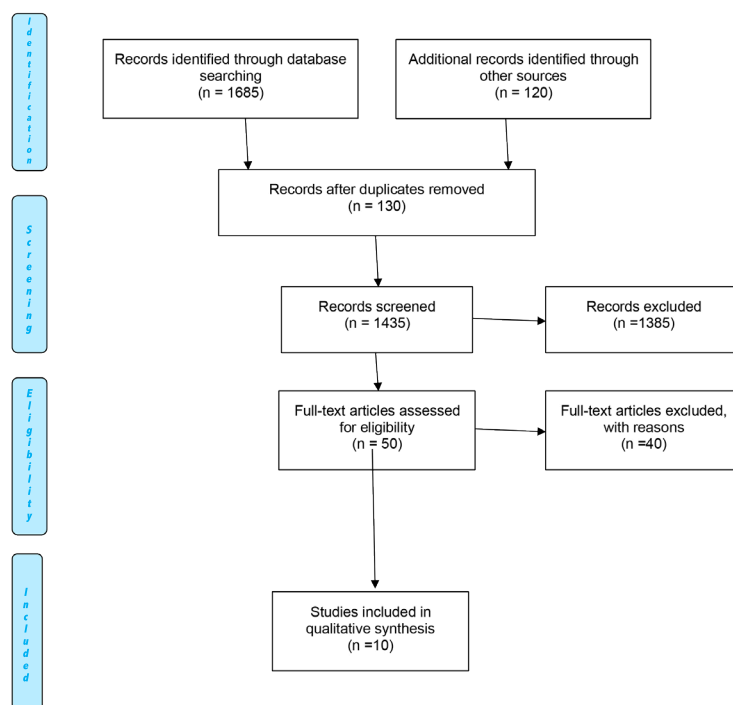


Figure 1: Study inclusion and exclusion flowchart.

RESULTS

Coronary The systematic search of the databases identified a total of 1,686 potentially relevant articles. After the removal of duplicates and the application of inclusion and exclusion criteria, 10 studies were included in this systematic review, comprising 6 randomized clinical trials, 2 systematic reviews with meta-analysis, 1 feasibility trial, and 1 retrospective study, totaling 5,246 participants.

The studies were published between 2016 and 2025, with the mean age of participants ranging from 53 to 85 years. Seven studies focused on total knee arthroplasty (TKA), two on total hip arthroplasty (THA), and one included both procedures. According to the Oxford classification, two studies presented level 1a evidence, six studies were classified as level 1b, and two studies as level 2b.

Figure 1: Study inclusion and exclusion flowchart.

AUTHOR/YEAR	TYPE OF STUDY	SAMPLE	INTERVENTION	RESULTS	LEVEL OF EVIDENCE
Ueyama et al., 2023	Double-blind RCT	n=52 (unilateral TKA)	EAA 9 g/day vs placebo (lactose), 1 week pre-op + 2 weeks post-op	Rectus femoris muscle area: 134% vs 114% (p<0.05); Quadriceps strength: 159% vs 125% (p<0.05) at 2 years	1b
Dreyer et al., 2018	Double-blind RCT	n=39 (primary TKA, 53–76 years)	EAA 20 g twice daily vs placebo, 7 days pre-op + 6 weeks post-op	Quadriceps volume in the operated leg: -8.5% vs -13.4% (p=0.033); Contralateral quadriceps volume: -1.5% vs -7.2% (p=0.014)	1b
Lai et al., 2025	RCT	n=90 (TKA + T2DM)	Oral CHO 2 h or 4 h pre-op vs placebo	Insulin resistance at 2 h: 9.0 ± 3.4 vs 30.9 ± 10.5 (p<0.001); Postoperative hyperglycemia: 12% vs 34% (p<0.01)	1b
Alito & Aguilar-Nascimento, 2016	RCT	n=32 (THA, 26–85 years)	ACERTO protocol + immunonutrition (Impact® 600 mL/day, 5 days pre-op) vs traditional care	Length of hospital stay: 3 vs 6 days (p<0.01); Lower postoperative CRP in the intervention group (p<0.01)	1b
Khani et al., 2025	Systematic review and meta-analysis	n=903 (19 studies, TKA/THA)	Oral or IV protein/amino acid supplementation vs control	Quadriceps mass: MD 0.69 (95% CI 0.44–0.95); Hamstring mass: MD 1.04 (95% CI 0.52–1.55); No significant difference in strength	1a
Pradhan et al., 2025	Systematic review and meta-analysis	n=756 (10 studies, TKA/THA, 57–71.9 years)	Preoperative CHO vs control	Length of hospital stay: -0.47 days (95% CI -0.98 to 0.04, p=0.07); No significant differences in pain, nausea, or vomiting	1a
Simpson et al., 2019	Feasibility RCT	n=60 (TKA, 66.8 ± 8.6 years)	Multimodal package: weight loss + exercise + insoles + analgesia (12 weeks) vs standard care	Weight loss: 11.2 kg vs 1.3 kg (p<0.001); Improved quality of life (0.078 ± 0.195); Adherence 94%	2b
Kadado et al., 2022	RCT	n=153 (primary TKA)	CHO vs placebo vs control (no beverage)	No differences in pain, nausea, or length of hospital stay; 90-day readmission: 0% vs 5.9% vs 11.5% (p=0.047)	1b
Gonçalves et al., 2020	Retrospective study	n=3,015 (older adults, TKA/THA)	Immunonutrition (200 mL three times daily, 5 days pre-op + 5 days post-op) vs control	Length of hospital stay: 32.0 ± 19.4 h vs 56.0 ± 26.4 h (p<0.001); Infectious complications: 2.2% vs 4.6% (p<0.001); OR 0.45 (95% CI 0.30–0.68)	2b
He et al., 2022	RCT	n=94 (TKA, >65 years)	OECNS (electrolytes + CHO) 2 h pre-op vs traditional fasting	Preoperative hunger: 0.43 ± 0.10 vs 1.19 ± 0.21 (p<0.05); Anxiety: 9.04 ± 2.71 vs 11.21 ± 3.02 (p<0.05); POD1 hyponatremia: 6.4% vs 21.3% (p=0.036)	1b

RCT = Randomized Controlled Trial; TKA = Total Knee Arthroplasty; THA = Total Hip Arthroplasty; EAA = Essential Amino Acids; CHO = Carbohydrates; T2DM = Type 2 Diabetes Mellitus; OECNS = Oral Electrolyte and Carbohydrate Supplementation; CRP = C-Reactive Protein; SMD = Standardized Mean Difference; CI = Confidence Interval; OR = Odds Ratio.

DISCUSSION

Two double-blind randomized clinical trials (level 1b) specifically evaluated essential amino acid supplementation. Ueyama et al.⁶ demonstrated that supplementation with 9 g/day for 3 perioperative weeks resulted in superior recovery of rectus femoris muscle area at 2 years and improved quadriceps strength.

Dreyer et al., using a higher dose (20 g twice daily) over a longer period (7 days preoperatively plus 6 weeks postoperatively), observed significant preservation of muscle volume measured by magnetic

resonance imaging. The intervention group exhibited less loss of quadriceps volume in both the operated leg and the contralateral leg.⁷

The meta-analysis by Khan et al. (level 1a), including 19 studies with 903 patients, confirmed the benefits of protein and amino acid supplementation for preserving muscle mass. The analysis demonstrated a significant reduction in muscle atrophy of the quadriceps femoris and hamstrings. However, the effects on muscle strength were inconsistent, with no significant differences between groups.⁸

Lai et al. (level 1b) specifically evaluated 90 patients with type 2 diabetes mellitus undergoing TKA. Administration of oral carbohydrates 2–4 hours before surgery resulted in a dramatic reduction in postoperative insulin resistance.⁹ The group receiving carbohydrates 2 hours before surgery exhibited significantly lower insulin resistance compared with placebo, representing a 71% reduction. The incidence of postoperative hyperglycemia was also lower.

He et al. (level 1b) evaluated 94 older patients (>65 years) receiving combined electrolyte and carbohydrate supplementation (OECNS) 2 hours preoperatively. The results demonstrated significant improvement in perioperative comfort, with reductions in preoperative hunger, anxiety, and a lower incidence of postoperative hyponatremia.¹⁰

The meta-analysis by Pradhan et al. (level 1a), including 10 studies with 756 patients, did not demonstrate a statistically significant reduction in length of hospital stay with preoperative carbohydrate loading (mean difference of -0.47 days), although a favorable trend was observed. No significant differences were found in postoperative pain, nausea, or vomiting.¹¹

Alito and Aguilar-Nascimento (level 1b) demonstrated that the ACERTO protocol combined with immunonutrition (Impact® 600 mL/day for 5 preoperative days) resulted in a significant reduction in hospital stay (median of 3 vs. 6 days, $p < 0.01$) and lower postoperative C-reactive protein levels.¹²

Gonçalves et al. (level 2b), in a retrospective study involving 3,015 older patients, observed that perioperative immunonutrition significantly reduced length of hospital stay (32.0 ± 19.4 h vs. 56.0 ± 26.4 h, $p < 0.001$) and infectious complications (2.2% vs. 4.6%, $p < 0.001$). Logistic regression analysis demonstrated a 55% reduction in the likelihood of infectious complications.¹³

Kadado et al. (level 1b) evaluated 153 patients allocated to three groups (carbohydrates, placebo, and control). Although no differences were observed in immediate postoperative outcomes, a significant reduction in 90-day readmissions was found: 0% in the carbohydrate group versus 5.9% in the placebo group versus 11.5% in the control group.¹⁴

Simpson et al. (level 2b) evaluated a 12-week multimodal protocol including weight loss, exercise, insoles, and analgesic adjustment in 60 patients awaiting TKA. The intervention group achieved significant weight loss (11.2 kg vs. 1.3 kg, $p < 0.001$) and clinically meaningful improvements in health-related quality of life. Overall adherence was 94%, varying among the different components: exercise, weight loss, analgesic adjustment, and insoles.¹⁵

All 10 studies reported an adequate safety profile for the nutritional interventions. No serious complications related to supplementation were reported. Minor adverse events were rare and included mild gastrointestinal discomfort and transient nausea. Adherence to the protocols was consistently high, ranging from 91% to 100% among studies reporting this outcome.

Considerable heterogeneity was observed among studies regarding supplementation protocols, study populations, and methods used to assess outcomes. This heterogeneity was particularly evident in studies evaluating length of hospital stay and muscle strength, limiting the ability to perform meta-analyses.

Most studies had relatively short follow-up periods, with the exception of Ueyama et al. (2 years). The

durability of the benefits and their impact on long-term quality of life remain uncertain. Studies with extended follow-up are needed to establish the true value of these interventions.⁶

Based on the current evidence, differentiated protocols may be proposed:

For the General Population:

- Essential amino acids: 15–20 g/day, initiated 1 week preoperatively and maintained for 4–6 weeks postoperatively
- Preoperative nutritional assessment to identify patients at risk

For Patients with Diabetes:

- Mandatory carbohydrate loading: 2 hours before surgery
- Intensive glycemic monitoring during the first 24 hours
- Consideration of essential amino acid supplementation

For Older Patients (≥65 years):

- Immunonutrition: 5 preoperative days
- Electrolyte supplementation combined with carbohydrates
- Monitoring of electrolyte imbalances

For Patients with Overweight/Obesity:

- Multimodal preoperative protocol including weight loss, exercise, and optimization of comorbidities
- A 12-week preparation period whenever feasible

CONCLUSIONS

The evidence identified in this review indicates that perioperative nutritional interventions are safe and effective in improving multiple outcomes following hip and knee arthroplasty. The benefits are most consistent in the preservation of muscle mass and metabolic modulation, with emerging evidence supporting reductions in complications and improvements in patient experience. Personalizing interventions based on specific patient characteristics represents an opportunity to optimize benefits and establish nutritional supplementation as a standard component of perioperative care in arthroplasty.

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ERAS PROTOCOL IN CARDIAC SURGERY: AN UMBRELLA REVIEW OF SYSTEMATIC REVIEWS

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ABSTRACT

Introduction: Enhanced Recovery After Surgery (ERAS) protocols represent a multimodal perioperative approach designed to reduce surgical stress, minimize postoperative complications, and accelerate recovery in patients undergoing cardiac surgery. **Objective:** To analyze the scientific evidence regarding the effectiveness of ERAS protocols on perioperative outcomes in cardiac surgery. **Methods:** A literature review was conducted using the PubMed database. The search strategy included the descriptors “cardiac surgery” and “ERAS protocol”, combined with the Boolean operator AND. Systematic reviews published between January 2021 and April 2026, involving adult patients undergoing cardiac surgery, were included. **Results:** Twenty-one studies were identified, of which eight systematic reviews met the eligibility criteria, comprising a total of 48,248 patients. The evidence demonstrated that ERAS protocols were associated with shorter mechanical ventilation time, reduced intensive care unit and hospital length of stay, fewer perioperative complications, and improved postoperative recovery. Multimodal analgesia and multidisciplinary care were identified as key components of successful ERAS implementation. **Conclusion:** ERAS protocols have shown the potential to improve perioperative recovery in cardiac surgery by reducing mechanical ventilation time, intensive care unit and hospital stay without increasing mortality. However, the heterogeneity of existing protocols and the low certainty of the available evidence highlight the need for well-designed multicenter randomized controlled trials to standardize their implementation and confirm their clinical benefits.

Keywords: Anesthesiology, Enhanced Recovery After Surgery, Cardiac Procedures, Perioperative Care, Thoracic Surgery.

INTRODUCTION

The implementation of Enhanced Recovery After Surgery (ERAS) protocols has become one of the fundamental pillars of contemporary perioperative care. By proposing a multimodal, interdisciplinary, and patient-centered approach, the ERAS protocol aims to attenuate the metabolic response to surgical stress, reduce complications, and accelerate functional recovery.¹ Although well established across several specialties, its application in cardiac surgery is of critical relevance, given the growing volume of procedures, combined with the profile of patients with multiple

comorbidities and high clinical complexity, which contributes to high postoperative morbidity and substantial healthcare resource utilization.²

Historically, initiatives aimed at enhanced recovery in cardiac care evolved from the Fast-track concept, initially focused on early extubation, toward an integrated care model.³ Currently, the effectiveness of these strategies depends on a structured organization encompassing the preoperative, intraoperative, and postoperative phases.⁴ In intraoperative management, the selection of the anesthetic technique plays a central role. Evidence suggests that techniques such as spinal anesthesia may offer significant benefits, including reduced bleeding, improved pain control, and decreased opioid requirements, which, consequently, may contribute to a shorter duration of mechanical ventilation.⁵

The safe transition to Fast-track extubation is determined by key factors such as hemodynamic stability, adequate reversal of neuromuscular blockade, and the patient's baseline functional status.² Meta-analyses indicate that early extubation, when appropriately indicated, is a safe technique that does not increase perioperative complication rates and has the potential to reduce hospital length of stay and operational costs.³ In this context, the role of the multidisciplinary team is essential to ensure adherence to protocols and patient safety.¹

Given the need for standardization, expert groups, including cardiovascular anesthesiologists, intensivists, and surgeons, have sought to synthesize the available evidence.⁵ It is essential to examine the literature with the aim of resolving contradictions found in randomized clinical trials and establishing consensus regarding the impact of anesthetic techniques and early extubation on clinical outcomes. Therefore, this review article aims to analyze the current state of ERAS protocols in cardiac surgery, discussing their implications for optimizing recovery and healthcare system efficiency.

METHOD

A literature review was conducted in the PubMed database. The keywords used for the search were "cardiac surgery" and "ERAS protocol". The keywords were combined using the Boolean operator AND (for different terms).

The articles were selected when they met the following inclusion criteria: publication between January 2021 and April 2026, in English; a methodological design comprising a systematic review with a human sample, involving adult patients aged at least 18 years.

Studies that did not address the use of the ERAS protocol in cardiac surgery and studies for which full-text access was not possible were excluded.

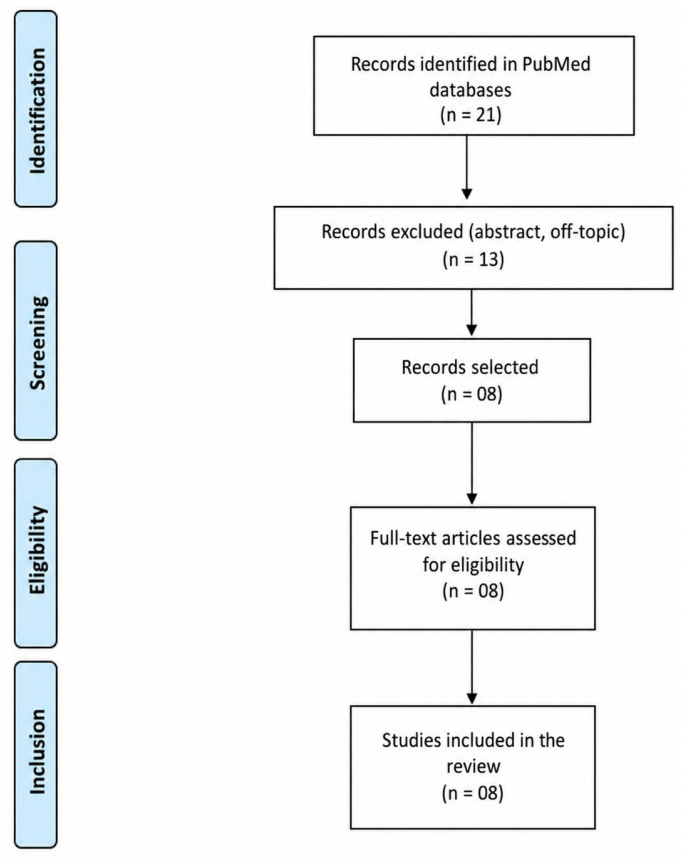


Figure 1 : Flowchart demonstrating the selection of articles.

RESULTS

Initially, 21 articles were found. After reading the abstracts, 13 articles that did not meet the inclusion criteria were excluded. The remaining 8 articles (comprising a total of 48,248 patients) were assessed for eligibility and subsequently included in the review.

Data regarding the included articles can be seen in Table 1.

Figure 1 : Summary of the included articles, with their objectives and main conclusions.
 ERAS: Enhanced Recovery After Surgery; FT: Fast-Track; RCTs: randomized clinical trials.

Author/Year	No. of participants	Objective	Conclusion
Hoogma et al. / 2025 (3)	2625	To compare whether ERAS is superior to FT in cardiac surgery, especially regarding length of hospital stay and patient recovery.	ERAS programs may reduce ICU and hospital length of stay, as well as the duration of mechanical ventilation. ERAS programs that include preoperative, intraoperative, and postoperative interventions are superior to fast-track strategies that act only during the intraoperative period.
Spadaccio, et al. / 2024 (6)	1.704	To analyze all randomized studies applying ERAS-like protocols in cardiac surgery with regard to perioperative outcomes.	ERAS-like protocols have no impact on short-term survival after cardiac surgery, but allow earlier hospital discharge while reducing surgical complications. However, this study demonstrates non-adherence and heterogeneity regarding the entirety of ERAS protocols, which justifies the need for further RCTs in this area, including a greater number of reference elements.
Aguero-Martins, et al. / 2021 (7)	5.059	To estimate the effectiveness of enhanced recovery protocols on the perioperative course of patients undergoing cardiac surgery.	Enhanced recovery protocols in cardiac surgery improve the quality of care, as evidenced by a reduction in perioperative complications and a decrease in the incidence of hospital readmission in the month following surgery.
Goecke et al. /2025 (8)	1287	To analyze how ERAS protocols are applied in minimally invasive valve surgery and assess their impact on perioperative outcomes and patient recovery.	ERAS protocols and minimally invasive valve surgery act synergistically to improve recovery and reduce hospital length of stay. Standardization of ERAS protocols for minimally invasive valve surgery may enhance these benefits and increase their adoption.
Malvindi et al. / 2024 (9)	5142	To reduce postoperative complications and promote earlier recovery. The aim is to assess the current status and implementation of ERAS protocols in patients undergoing heart valve surgery and to summarize	The adoption of structured ERAS protocols has the potential to improve outcomes in patients undergoing heart valve surgery. Further evidence with larger populations is needed, including more homogeneous protocols and the assessment of additional outcomes, such as patient satisfaction, recovery, and quality of life after surgery.

		the associated clinical outcomes.	
Heybati, et. al. / 2023 (10)	26.257	To compare the relative efficacy of non-opioid adjuvant analgesic regimens in adult patients undergoing cardiac surgery.	The data suggest broader use of non-opioid adjuvants to minimize pain and improve recovery.
Zhang et al. / 2021 (11)	1705	To assess the current evidence on the efficacy of ERAS protocols in cardiac surgery, determining whether they improve patient outcomes.	The evidence is limited by the lack of high-quality randomized clinical trials. The absence of implementation of Class I interventions recommended by the ERAS Cardiac Society was observed.
Diz-Ferreira, et al. / 2025 (12)	4.469	To assess the impact of ERAS programs in cardiac surgery on hospital length of stay, mortality, atrial fibrillation, and quality of life.	ERAS programs have been associated with reduced hospital length of stay and have not demonstrated differences in mortality or atrial fibrillation; the quality of the evidence was considered very low. To recommend the implementation of ERAS programs in cardiac surgery, randomized studies providing evidence of their efficacy are needed, as well as studies that include quality of life and other outcomes centered on patient recovery.

DISCUSSION

The findings accumulated in the recent literature demonstrate that the implementation of ERAS protocols in cardiac surgery has shown highly promising results. A significant reduction in intensive care unit (ICU) length of stay, overall hospital length of stay, and the incidence of postoperative complications has been consistently observed, without this implying an increase in mortality rates.⁶⁻⁷ However, although such clinical benefits are reported with relative consistency, the literature still suffers from important methodological limitations that prevent definitive conclusions regarding the actual impact of the protocol in its entirety.

The main obstacle to the consolidation of this evidence lies in the marked lack of standardization of the clinical care protocols used. Under the ERAS acronym, a large proportion of studies group markedly heterogeneous institutional strategies, with the isolated adoption of only some perioperative components being frequent, to the detriment of the complete and systematic implementation of the guidelines proposed by the ERAS Society.^{6,8,9,10} This conceptual and methodological disconnect not only hinders direct comparability among clinical trials but also makes it difficult to isolate and identify which specific interventions are effectively responsible for the favorable outcomes observed.

It therefore becomes evident that the therapeutic success of ERAS is intrinsically linked to the synergistic and simultaneous combination of multiple evidence-based interventions, going beyond the mere application of fragmented measures. From this perspective, the protocol differs substantially from traditional Fast-Track strategies, whose scope is frequently restricted to optimization of the intraoperative period focused on early extubation.³⁻⁷ Although reducing the duration of mechanical ventilation represents a relevant outcome, it is insufficient, in isolation, to mitigate overall surgical stress and accelerate patient recovery. It is the cumulative and multimodal effect resulting from the integration of preoperative education, opioid-sparing multimodal analgesia, early mobilization, early feeding, anesthetic optimization, and rehabilitation that culminates in substantial improvement in clinical outcomes.³⁻⁷

This operational divergence between Fast-Track and ERAS represents a true paradigm shift in perioperative care.³⁻⁷ While the former aims to accelerate linear and specific stages of recovery, the ERAS model advocates an integrated and continuous approach that interconnects the preoperative, intraoperative, and postoperative periods.³⁻⁷ The central objective shifts toward attenuating the inflammatory and metabolic response resulting from surgical trauma, aiming to preserve physiological homeostasis and promote early functional recovery of the individual.³⁻⁷

In the context of minimally invasive cardiac surgery, this conceptual correlation reaches an even more significant level. The reduced tissue trauma inherent to these surgical approaches acts synergistically with ERAS measures, enhancing the reduction in ICU and ward length of stay, enabling early hospital discharge, and promoting substantial optimization of healthcare system operating costs.⁸ Despite the relevance of these findings, the available body of evidence remains limited due to the predominance of studies with small population samples, heterogeneous methodological designs, and disparities in practical implementation processes, highlighting the urgent need for multicenter investigations with greater scientific robustness.⁸⁻⁹

ERAS protocols in cardiac surgery have shown an association with reduced hospital length of stay, although the certainty of the evidence was considered very low. No significant differences were observed in perioperative mortality or in the incidence of postoperative atrial fibrillation.¹²

Alongside logistical and organizational adjustments, optimization of pain management emerges as one of the most critical pillars for the success of the protocol. The implementation of multimodal analgesic regimens, characterized by a drastic restriction in opioid use, has provided solid benefits in pain control, reduction in the duration of ventilatory support, and acceleration of functional rehabilitation. Adjuvant drugs such as acetaminophen, magnesium, dexmedetomidine, gabapentin, clonidine, ketamine, and hydrocortisone have become key elements in achieving these goals.¹¹

Despite the theoretical robustness and favorable results, the translation of ERAS into everyday clinical practice remains one of the greatest contemporary challenges. Cultural barriers, expressed as resistance to change among healthcare teams, the requirement for highly integrated multidisciplinary coordination, limitations in healthcare service infrastructure, and disparities in the allocation of financial and material resources impose severe obstacles to the establishment of the protocol. Thus, it can be inferred that the main current bottleneck does not lie in the validity or efficacy of the ERAS concept itself, but rather in the ability of healthcare services to ensure its systematic and uniform application.⁷⁻⁸

Given this scenario, a clear consensus emerges in the literature regarding the urgent need for new randomized, multicenter clinical trials based on strictly standardized protocols that encompass all recommendations issued by the ERAS Society. In addition to measuring classical clinical and surgical outcomes, future investigations need to incorporate indicators centered on patients'

perspectives, such as quality-of-life scales, speed of functional recovery, satisfaction levels, and time to return to usual activities. Only through this expansion of the evaluative scope will it be possible to accurately quantify which specific ERAS components exert the greatest detrimental or beneficial impact on the recovery journey after cardiac surgery.^{6, 9, 10}

CONCLUSION

The implementation of the ERAS protocol in cardiac surgery represents a consistent evolution in perioperative care, demonstrating efficacy in optimizing relevant clinical outcomes, such as reducing the duration of mechanical ventilation, ICU length of stay, and hospital length of stay, as well as mitigating postoperative complications without compromising safety or increasing mortality rates. The success of this strategy lies in its multimodal and synergistic nature, overcoming the limitations of traditional Fast-Track approaches. However, the consolidation of the protocol as the gold standard of care faces critical challenges, centered on the methodological heterogeneity of current studies and low adherence to the entirety of international guidelines. For the benefits of ERAS to be widely validated and replicated in routine surgical practice, high-quality multicenter randomized clinical trials are needed. These studies should focus on the standardization of perioperative interventions and include outcomes centered on the patients' own experience, such as quality of life and early functional recovery.

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