

Residência de Anestesiologia do Serviço de Anestesia e Medicina Perioperatória do Hospital de
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**MORTALIDADE INTRA-HOSPITALAR EM PACIENTES SUBMETIDOS A CIRURGIA EM
UM HOSPITAL UNIVERSITÁRIO NO SUL DO BRASIL: COMPARAÇÃO ENTRE DUAS
COORTES - ANTES E DURANTE A PANDEMIA COVID-19**

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LISTA DE ABREVIATURAS

ASA-PS: American Society of Anesthesia – Physical Status

CI – Confidence interval

FTR – Failure to Rescue

IC – Intervalo de confiança

LMIC – Low-middle income country

RR – Risco relativo

SD – Standard deviation

Resumo

Introdução: A pandemia de COVID-19 influenciou drasticamente a prática médica no nosso país. Alterações na dinâmica do funcionamento dos hospitais foram imprescindíveis para reduzir a sobrecarga e para evitar o colapso do sistema de saúde. O presente estudo objetiva examinar se a pandemia impactou na mortalidade de pacientes cirúrgicos no período perioperatório até 30 dias em um hospital referência para o tratamento da COVID-19 no sul do Brasil.

Métodos: Conduzimos um estudo de coorte utilizando dados de pacientes cirúrgicos que foram operados antes (janeiro de 2018 a dezembro de 2019) e durante a pandemia do novo coronavírus (fevereiro a dezembro de 2020). Três grupos de pacientes submetidos à cirurgia foram criados: Pré-pandemia (2018-2019), Durante Pandemia COVID-negativos e Durante Pandemia COVID-positivos (2020). Estimamos o risco clínico e cirúrgico e associações independentes entre a pandemia e mortalidade intra-hospitalar até 30 dias foram avaliadas utilizando o modelo de regressão de Poisson com variância robusta.

Resultados: Foram incluídos 15.156 pacientes no estudo, sendo 12.207 pertencentes ao grupo pré-pandemia e 2.949 aos grupos de durante a pandemia. A mortalidade encontrada foi de 2,5% (309/12207) no grupo controle versus 7,2% (212/2949) no grupo operado durante a pandemia. A mortalidade entre pacientes diagnosticados com COVID durante ou após a cirurgia foi de 25,8% (32/124) ao passo que dentre os negativos para COVID foi de 6,4% (180/2816). A proporção de cirurgias urgentes, ASA \geq 3 foi maior no grupo da pandemia. O risco relativo de ter sido submetido a cirurgia durante a pandemia, após ajustes para variáveis sabidamente relacionadas com mortalidade foi de 1,52 (IC 95% 1.27-1.84). Associações independentes foram encontradas entre mortalidade e categoria do modelo de risco Ex-Care, infecção por COVID e cirurgia torácica. Análise de sensibilidade excluindo pacientes infectados por COVID permaneceu mostrando aumento do risco cirúrgico no período da pandemia. [RR de 1.50 (95% IC 1.27-1.78)].

Resultados: A mortalidade perioperatória foi substancialmente aumentada dentre submetidos à cirurgia na pandemia, mesmo entre aqueles sem infecção por COVID. Dessa forma, nosso resultado sugere que a pandemia impactou negativamente na assistência à saúde. Esta pandemia sem precedentes reforça a necessidade de se adotarem estratégias que fortaleçam o sistema cirúrgico e promovam prosperidade econômica em países de baixo e médio rendimentos, tal como o Brasil.

Palavras-chave: COVID, mortalidade perioperatória,

Abstract

Before the pandemic, healthcare systems in LMICs (low-middle income countries) already experienced limited 'capacity to rescue' and scaling up of care to prevent deaths in those patients who develop postoperative complications and physiological deterioration on hospital wards. It is still uncertain whether the pandemic itself and hospital delivery have played a role in raising postoperative mortality rates even further. This before and after cohort study aimed to assess the pandemic impact on postoperative mortality up to 30 days in a university, COVID-19 referral hospital, in Southern of Brazil.

Methods: We conducted a cohort study using data from patients who operated before (from January 2018 to December 2019) and during the pandemic (from February to December 2020). Data describing the two groups were compared. The surgical and clinical risk were estimated, and the independent association of pandemic and in-hospital 30-day mortality were evaluated using Poisson regression with robust error variance analysis.

Results: 15.156 patients were included, 12.207 operated before the pandemic and 2.949 operated during the first pandemic year. Mortality rates were 2,5% (309/12207) in the control group versus 7,2% (212/2949) in during pandemic group. Mortality among COVID-positive patients was 25,8% (32/124) and between COVID-negative patients was 6,4% (180/2816). The proportion of urgent surgeries, ASA \geq 3 was higher in pandemic group. The relative risk of being operated during the pandemic, after adjustments for variables known to relate to mortality was 1,52 (1.27-1.84). Sensitivity analysis excluding COVID-positive patients showed the increase in mortality risk of being operated during pandemic [RR of 1.50 (95% CI 1.27-1.78)].

Conclusions: Postoperative mortality was substantially increased among patients submitted to surgery during the pandemic, even among those without COVID infection, and that suggests that the pandemic itself played a negative role in health surgical system. This episode in global health has reinforced the need to adopt strategies to strengthen surgical systems to save lives and promote economic growth in LMIC.

Key-words: postoperative mortality; surgical death; surgical risk, pandemic, COVID-19, Coronavirus;

1. INTRODUÇÃO

O Brasil enfrentou desafios significativos durante a pandemia do coronavírus. Logo no início da pandemia no Brasil o Hospital de Clínicas de Porto Alegre foi apontado como hospital de referência regional para o tratamento de pacientes criticamente enfermos com COVID-19. Apesar de aumentar o número de leitos de UTI em 217%¹, admissões de COVID-19 ultrapassaram a capacidade operacional e pacientes críticos tiveram que ser tratados fora da UTI. A instituição passou por uma reorganização de processos e estrutura para desenvolver um modelo de atendimento para pacientes com COVID-19 flexível que pudesse se expandir com base na necessidade diária. A instituição conseguiu aumentar o número de leitos e de profissionais dedicados, melhorar o monitoramento do paciente, instituir uma equipe de suporte ventilatório na enfermaria e garantir a continuidade dos cuidados 24 horas por dia, 7 dias por semana. As lições aprendidas no exterior e nos primeiros dias da pandemia levaram a construção de uma enfermaria capaz de se adaptar para atender pacientes críticos fora da UTI. Além disso, as atividades cirúrgicas foram extremamente restritas no período, sendo operados apenas pacientes com condições urgentes. Cirurgias eletivas foram suspensas por vários meses, sendo que as salas de recuperação pós-operatórias foram transformadas em leitos de terapia intensiva, e os profissionais anestesistas deslocados de sua função para o atendimento de pacientes fora do bloco cirúrgico.

Dentro dessa nova realidade faz-se necessário compreender o impacto da pandemia no sistema cirúrgico. Ter um sistema voltado ao atendimento de uma pandemia certamente impacta na redução da qualidade de atendimento em outros setores. Os pacientes não tiveram suas condições atendidas em tempo hábil, sendo possivelmente operados em condições avançadas de suas doenças. Além disso, aqueles que foram operados experimentaram modificações nas rotinas de atendimento e processos em todos os serviços do hospital.

A fim de entender o impacto da pandemia comparamos os desfechos cirúrgicos em 2 coortes de pacientes: operados antes da pandemia e durante a mesma, controlando para fatores sabidamente associados ao risco cirúrgico.

2. REVISÃO DA LITERATURA

2.1 Busca Bibliográfica

A revisão da literatura incluiu a busca por periódicos indexados publicados desde janeiro de 2000. Além disso, foram incluídos documentos de políticas governamentais internacionais que abordam os principais fatores de risco para morbimortalidade perioperatória, conforme o quadro 1.

Quadro 1. Metodologia da busca bibliográfica

	Cuidados perioperatórios, failure to rescue, mortalidade
Palavras-chave (português)	cirúrgica, complicações pós-operatórias, pandemia. COVID 19. coronavirus
Palavras-chave (inglês)	surgical mortality, failure to rescue, perioperative mortality, COVID-19, coronavirus, SARS-COV-2, surgical death
Bases de Dados	Pubmed

2.2.1 Fatores de Risco Perioperatórios relacionados ao paciente

2.2.1.1 Idade

Sabe-se que o aumento da idade continua sendo um importante fator de risco para morbimortalidade pós-operatória². A mortalidade da população geral é de cerca de 1,02%. Nos pacientes com idade entre 60 e 69 anos a mortalidade é de 2,2%, nos de 70-79 anos é de 2,9%, nos acima de 80 anos é de cerca de 5,8 a 6,2% e naqueles com mais de 90 anos é de 8,4%³. No entanto, não é a idade por si só que leva a um risco aumentado de mortalidade e sim o declínio das funções corporais que advêm com o avanço da idade. O impacto desse declínio foi muito bem avaliado e demonstrado pelo escore de *Frailty*⁴, que tem sido associado à expectativa maior de desfechos adversos após cirurgia, incluindo mortalidade, declínio funcional e complicações cardíacas.

Usar um critério baseado unicamente em idade é simplista. O envelhecimento compreende um processo progressivo descrito como a manutenção da vida com uma capacidade de ajustamento diminuída, associada a mecanismos adaptativos e homeostáticos prejudicados, resultando em uma suscetibilidade crescente aos efeitos do estresse⁵.

Idosos formam um segmento populacional em expansão em países desenvolvidos. É o segmento populacional com o mais rápido crescimento nos Estados Unidos. O Censo Americano projeta que em 2050 irão representar mais de 21% da população, contra os cerca de 13% atuais⁶. Acredita-se que os adultos que atualmente estão envelhecendo entrarão nos seus anos geriátricos melhores e mais saudáveis do que as gerações precedentes. Uma significativa parte desse segmento irá demandar cuidados cirúrgicos durante sua vida, sendo uma preocupação para os serviços de saúde⁷.

Atualmente, cerca da metade de todas as cirurgias nos Estados Unidos são realizadas em pacientes com mais de 65 anos de idade. Esta população de pacientes é de alto risco para morbidade, mortalidade e aumento de custos. A incidência de complicações eleva em

até 26% a mortalidade pós-operatória em pacientes com mais de 80 anos. Entre o crescente grupo populacional cirúrgico de pacientes com 65 anos ou mais, o subgrupo de crescimento mais rápido é dos indivíduos maiores de 85 anos. Por conseguinte, um maior número de indivíduos se apresenta para cirurgia com condições relacionadas à sua idade avançada⁴.

Em contrapartida, um estudo retrospectivo canadense sugere que idade maior de 80 anos não é preditor de aumento de morbidade e mortalidade após cirurgia de urgência, mas sim o escore de ASA como fator isolado mais importante⁶, sugerindo que as comorbidades têm mais impacto na morbidade e mortalidade perioperatória do que a idade em si⁷.

Além de uma maior taxa de mortalidade pós-operatória, a população idosa também apresenta maiores taxas de *failure to rescue* (FTR) – morte precedida por uma complicação pós-operatória (figura 1) –, que pode ser atribuído a uma menor reserva fisiológica e capacidade de resposta ao *stress*⁸.

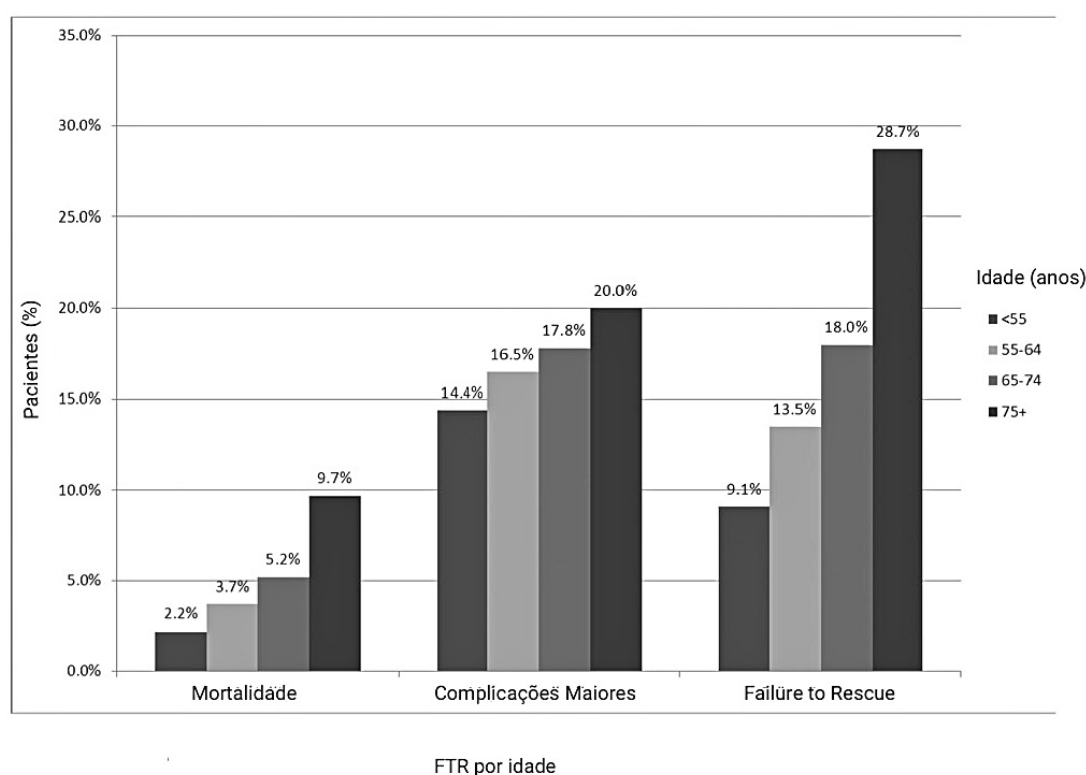


Figura 1. Taxas de mortalidade, complicações maiores e FTR em diferentes grupos etários.

Fonte: Modificado de Ghaferi et al⁸.

2.2.1.2 A escala ASA-PS

O estado físico do paciente determinado pelo índice ASA tem sido correlacionado ao risco de mortalidade perioperatória e é mundialmente utilizado para este fim^{9,10}.

A classificação ASA-PS se relaciona positivamente com a probabilidade de óbito pós-operatório em até 48 horas¹¹. Ela foi usada como principal variável clínica em um modelo de risco recentemente desenvolvido com uma análise de 298.772 pacientes submetidos a cirurgia não-cardíaca, usando dados do *American College of Surgeons National Surgical*

Quality Improvement Program database. Esse modelo apresentou alta acurácia na predição de morte em até 30 dias no pós-operatório (C statistic 0,897)¹².

Um outro estudo, realizado com pacientes submetidos a cirurgias eletivas e de emergência, examinou a força da associação entre índice ASA-PS e desfechos pós-operatórios, concluindo que houve aumento significativo da mortalidade intra-hospitalar conforme o status ASA-PS e também de complicações como perda sanguínea, tempo de ventilação no pós-operatório, tempo de internação em UTI, complicações pulmonares e cardíacas¹³.

2.2.2 Fatores de Risco Perioperatórios relacionados ao procedimento

2.2.2.1 Cirurgia de urgência X eletiva

Cirurgias de urgência e emergência correlacionam-se positivamente com uma maior mortalidade pós-operatória^{13,14} mesmo garantido o acesso imediato às instalações cirúrgicas¹⁵.

Um estudo de coorte dinamarquês com 2889 pacientes submetidos a colectomia total mostrou que 1% dos pacientes submetidos à cirurgia eletiva morreram enquanto 5,3% dos pacientes submetidos a cirurgia de emergência tiveram o mesmo desfecho. Para os pacientes com 60 anos ou mais, a mortalidade aumentou para 3,3% nos submetidos à colectomia eletiva e para 18,4% para em caráter de emergência¹⁶.

Um trabalho realizado em um hospital geral terciário brasileiro entre 1996 e 2005 envolvendo 53.718 procedimentos anestésicos descreveu o estado físico ASA-PS e a cirurgia de emergência como fatores de risco maiores para ocorrência de parada cardíaca relacionada à anestesia. Este estudo também observou uma incidência 11,27 vezes maior de parada cardíaca em cirurgia de emergência do que em cirurgias eletivas e uma incidência 25,5 vezes maior em pacientes ASA IV do que em pacientes ASA- PS I¹⁷.

A maioria dos sistemas de pontuação de risco cirúrgico reconhece o peso que uma cirurgia não-eletiva tem na mortalidade. Por exemplo, o escore da Sociedade Americana de Anestesiologia (ASA) inclui um sufixo "E" para designar uma cirurgia de emergência, compreendendo uma avaliação subjetiva de maior risco. Os escores POSSUM (*Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity*), APACHE (*Acute Physiology and Chronic Health Evaluation*), o modelo S-MPM (*Surgical Mortality Probability Model*)¹¹, o IRIS score (*Identification of Risk In Surgical patients*)¹⁸ e a escala *The Surgical Risk Scale*¹⁹ também atribuem um maior risco de morte se o modo de admissão não é eletivo²⁰.

2.2.2.2 Porte Cirúrgico

Apesar de o impacto do porte da cirurgia na morbimortalidade não ser comumente avaliado de forma isolada, é uma variável que reflete o peso do trauma cirúrgico e da consequente resposta orgânica ao estresse, levando em conta o grau de invasão do procedimento e o risco de sangramento¹³.

O porte cirúrgico é considerado uma variável em vários escores de risco, como por exemplo o Escore de Risco Cardíaco Modificado²¹. O *Surgical Risk Scale* utilizou a classificação de porte cirúrgico inglesa *BUPA (British United Provident Association)*, que divide os procedimentos em maiores, intermediários e menores²². Já o Modelo de Probabilidade de Mortalidade Cirúrgica (S-MPM) classificou os procedimentos em maiores, intermediários e menores através de estimativas empíricas de mortalidade após ajustes para o ASA e estado de emergência ou eletiva¹².

2.3 Instrumentos de classificação de risco → Risco Ex-care:

A partir de um antigo modelo de risco perioperatório (Risco SAMPE) do Serviço de Anestesiologia do Hospital de Clínicas de Porto Alegre, foi desenvolvida pelo mesmo serviço uma ferramenta (Ex-Care)²³ baseada em 4 variáveis: idade do paciente, escore ASA, natureza e porte do procedimento. Tal escore de risco se mostrou mais eficaz que o RCRI (Revised Cardiac Risk Index) e o ASA-PS isoladamente e tão eficaz quanto modelos validados como SORT (Surgical Outcome Risk Tool) e o CCI (Charlson Comorbidity Index), porém necessita de um menor número de variáveis para seu cálculo. Possui grande importância por prever mortalidade no perioperatório e pode ser usado como triagem para organização de protocolos de cuidados de pacientes de maior risco.

2.4 Fatores relacionados a estrutura e processos

O termo em inglês “*failure to rescue*” é o óbito decorrente de complicação relacionada ao cuidado médico. Pode também ser definido como a falta da capacidade do sistema de reconhecer e tratar uma complicação pós-operatória que causa óbito num período de até 30 dias da cirurgia²⁴.

Geralmente uma complicação única precede os outros eventos, e deve ser encarada como evento sentinela, que ocorre em média entre cinco e 10 dias precedentes à morte, e intervenção precoce pode reduzir as taxas de óbito. Isto reflete qualidade de atendimento prestado e vários fatores estão envolvidos na falta de reconhecimento deste evento sentinela. Uma das maneiras de identificar os pacientes com maior probabilidade de complicação é a estratificação de risco através de modelos de risco perioperatórios.

3. JUSTIFICATIVA

A pandemia trouxe um cenário inesperado ao hospital de Clínicas de Porto Alegre, que transformou-se rapidamente para atender pacientes críticos. A capacidade do atendimento foi ampliada às custas da redução da assistência usual prestada aos pacientes com outras doenças, como os pacientes cirúrgicos. Mesmo com movimento, reduzido as cirurgias permaneceram ocorrendo. Faz-se necessário entender como a pandemia afetou o sistema de saúde como um todo. Sabendo-se que o sistema cirúrgico alicerça grande parte dos tratamentos das doenças em geral, estudaremos o impacto da pandemia nos desfechos dos pacientes que foram a cirurgia comparado com pacientes operados antes da pandemia.

4. OBJETIVOS

Geral:

Analisar o impacto que a pandemia provocou na mortalidade no período perioperatório no Hospital de Clínicas de Porto Alegre em até 30 dias da cirurgia.

Específicos:

Avaliar a mortalidade pós-operatória em pacientes submetidos a cirurgia no período da pandemia em comparação com a mortalidade antes da pandemia.

Avaliar a mortalidade pós-operatória em pacientes COVID submetidos a cirurgia no período da pandemia.

Identificar se a pandemia é um fator independentemente associado a maior mortalidade no período pós-operatório em até 30 dias.

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The side effect of pandemic in post-operative mortality in a COVID reference Hospital in Southern of Brazil: a 'before and after' pandemic cohort study with 15.156 patients

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Short title: Post-operative mortality before and during COVID-19

INTRODUCTION

More than 600.000 deaths occurred only in Brazil¹ since the pandemic's beginning. Brazil is considered an upper-middle-income country, but multiple layers of geographical and socioeconomic inequalities exist in healthcare access and health outcomes². The initial spread of COVID-19 and deaths were mainly affected by patterns of socioeconomic

vulnerability, and North and Northwest regions were particularly affected. Hospital human resources measured by the number of ICU physicians per capita and the number of ICU beds per capita was roughly twice as high in the South region compared to the North region. These inequalities led to higher COVID-19 death rates in the most socioeconomically vulnerable states³. However, even wealthy institutions were shifted primarily to the mounting demands posed by the pandemic to the detriment of the other diseases.

Early on the pandemic, Hospital de Clínicas de Porto Alegre was appointed as a regional reference hospital to treat critically ill patients with Coronavirus-19 in the south of Brazil. Despite increasing the number of ICU beds, COVID-19 admissions surpassed operational capacity, and critical patients had to be treated outside ICUs, in clinical wards and inside areas previously occupied by Surgical Units. The institution increased the number of COVID-19 dedicated professionals and beds, improved patient monitoring, instituted a noninvasive ventilatory support team, and ensured 24-7 continuity of care and assertive transition of care communication. This flexible system provided the means to face the health care challenge⁴ but the short and long term consequences of these adaptative changes for the health system, including the surgical system, need to be evaluated. Non-urgent, low and intermediate surgeries were postponed, and the referral to specialized care became difficult. Even oncological procedures had to be delayed due to the lack of available places or hospital resources.

Before the pandemic, healthcare systems in LMICs already experienced limited 'capacity to rescue' and scaling up of care to prevent deaths in those patients who develop postoperative complications and physiological deterioration on hospital wards^{5,6}. It is still uncertain whether the pandemic itself and hospital delivery have played a role in raising postoperative mortality rates even further. Studies have proven that COVID-19 infection is an independent risk factor for increased perioperative mortality, with rates as high as 26%^{7,8}. However, the independent pandemic effect on health assistance and surgical outcomes need to be addressed.

In order to measure the effect of the COVID-19 pandemic in the surgical system of a referral public Hospital in Southern Brazil, we conducted a retrospective cohort study of surgical patients operated during the pandemic and compared it with a cohort of patients operated before the pandemic. We hypothesized that the surgical system was negatively impacted by the unprecedented pandemic with increased postoperative death rates in both COVID and non-COVID patients.

METHODS

The study protocol was approved by the Brazilian National Research Ethics Committee (CAAE 31063220400005327). The institutional review board approved the project with retrospective components to assess changes in care processes and clinical outcomes with a waiver for written informed consent, although a confidentiality agreement was signed to access the institution's database. The study is reported according to the STROBE guidelines.

Site

Hospital de Clínicas de Porto Alegre (HCPA), is a public tertiary care university teaching hospital in southern Brazil. Early in the pandemic, Brazil's federal government appointed HCPA as a regional reference hospital for the treatment of critically ill patients with COVID-19. The hospital increased its capacity to more than 200% and undergone several sequential adaptations to cover COVID patients. It was implemented 135 extra ICU beds from 62 before pandemic. Even though, the number of patients arriving surpassed any operational capacity and critical patients with acute respiratory failure had to be treated outside ICUs and the COVID dedicated ward was filled with patients requiring advanced respiratory support during peak months. The development and deployment of this plan required orchestrated actions such as a substantial increase in structure (new area was opened and equipped), and health workers were hired in an unprecedented quickness. Support of stakeholders, changing in assistance processes and regular training and workshops were fundamental to support the new reality. The majority of medical consultations were changed for virtual and surgical assistance was restructured according the pandemic flow. Still, overall Covid-19 mortality in our hospital was 23.0% by august 2021⁴.

Data source and study population

This is an observational single-center cohort using retrospective data from patients who underwent surgical treatment with a planned overnight hospital before pandemic, from January 2018 to December 2019, and during pandemic from March to December 2020 at Hospital de Clínicas de Porto Alegre. We did not include patients aged < 16 y, or those who underwent diagnostic or minor to intermediate procedures involving discharge from the hospital on the same day.

We collected data in our institutional health records and corrected for missing values using complete case analysis. Surgical data such as surgical specialty, surgical severity (major or non-major surgery) and nature of procedure (elective or non-elective) were collected, besides patient's demographic characteristics, COVID status and ASA-PS level. Surgical specialties were classified as follows: upper/lower gastrointestinal and hepatobiliary as general; breast, head & neck, gynecology, and plastics as other; and kept vascular,

orthopedic, urologic, thoracic, and neurosurgery as independent categories. COVID testing was performed in all in-patients undergoing surgery, following institutional guidelines. Patients were generally screened for COVID-19 with reverse transcriptase–polymerase chain reaction assay in nasopharyngeal swabs before surgery systematically after March 2020. Computed tomography or chest image were performed to investigate lung abnormalities when symptoms were present. Elective surgeries were postponed if COVID was confirmed or suspected.

Outcome Definition

The primary outcome was in-hospital postoperative mortality, censored at 30 days after surgery if the patient was still alive and in hospital.

Statistical analysis and variables adjustments

There are two groups of interest: before pandemic (control) and during pandemic cohort. Electronic case records included the same variables for both cohorts. For primary outcome data collection, we conducted a complete case analysis, excluding patients with missing data. Clinical data are shown as frequencies, mean (SD) or median (IQR). We used the Ex-care risk model⁹ to classify patients and according risk classes in both cohorts according the occurrence of the main outcome. The Ex-Care model was developed and validated with data from the same institution and included 4 variables demonstrably associated with postoperative mortality: age, American Society of Anesthesiology Physical Status [ASA-PS] classification, severity of the procedure, and nature of surgery. The resulting 30 day in-hospital mortality probability was categorized into four classes in order to be easily applied at the bedside: Class I, <2%; class II, 2-5%; class III, 5-10%; class IV, >10%. Classes III and IV were considered as high-risk surgical patients. A non-proprietary smartphone application is available on both Android and iOS platforms¹⁰.

We examined the independent association between in-hospital 30-day mortality for the two cohorts (before and during pandemic) using Poisson regression with robust error variance for primary outcome analysis. To control for potential confounding factors, we adjusted the model for a group of variables based on a conceptual framework describing the relationship between risk factors¹¹. Variables associated to patient's risk (ASA, age) and to surgical procedure entered in the model (urgent vs elective, major vs non-major and surgical specialty). We also built another model considering the Ex-Care risk model to control for an index of risk.

The calculation of a post-hoc power was planned after data analysis to verify the statistical power of the result with all predictors included in the final model. The significance

level for all analyses was 5%. Analysis was performed using the *Statistical Analysis System* (SAS Studio® 9.4) and *R* 3.5.1.

RESULTS

A total of 15.156 patients were included, 12.207 from before pandemic cohort years and 2.949 operated during the pandemic year (2020). Figure 1 describes patient inclusion within the study.

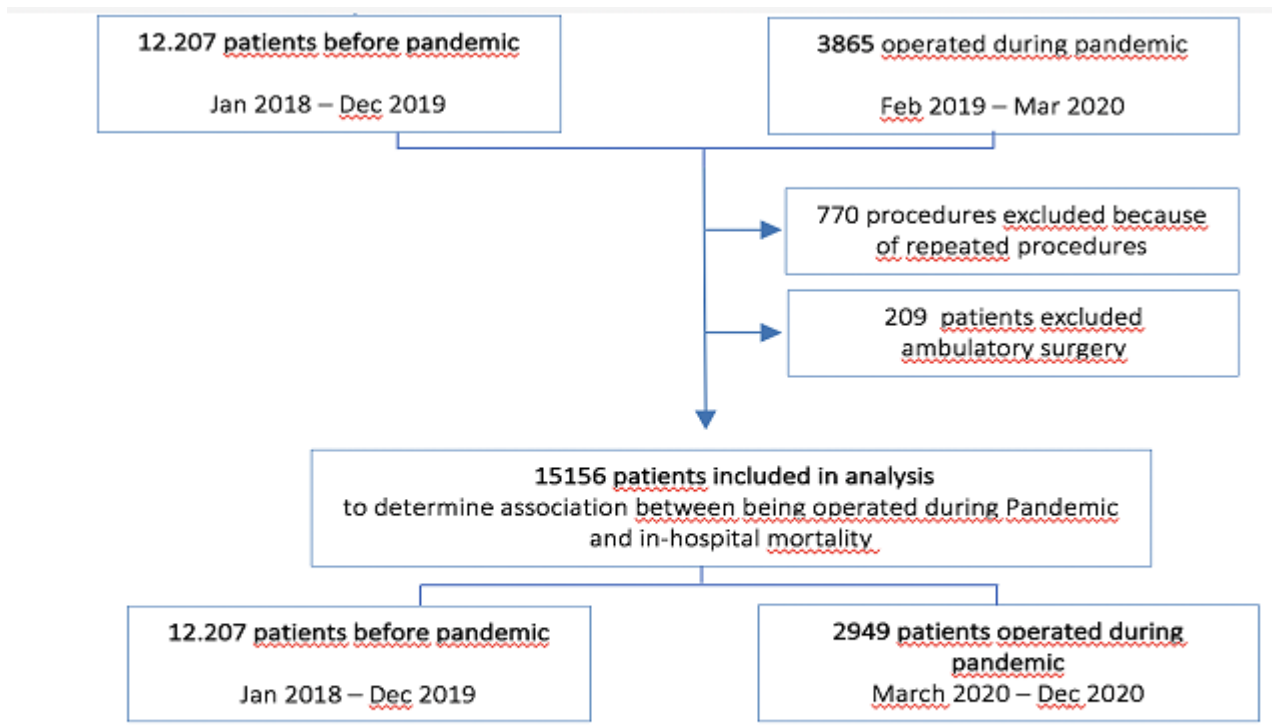


Figure 1. Flow diagram of study cohort selection

*procedures held at main surgical unit; OR: operating room

Patients from both cohorts had their mortality risk calculated according to the Ex-care risk model. We observed that patients with major risk were operated during pandemic. The proportion of high-risk patients (Predicted mortality 5,0-9,9%) was 4.8% in control and 8,5% in “pandemic group” and of very high-risk patients ($\geq 10\%$ 30-day risk of death) was 6.2% in “control” and 12% in “pandemic group”. Urgent surgeries occurred in 20,3% in control group versus 35,4% during pandemic group. Baseline characteristics of the study population according interest groups are shown in Table 1.

Table 1. Clinical characteristics, all patients and stratified by study group.

	Before pandemic (n=12207)	During Pandemic COVID negative (n=2949)	During Pandemic COVID positive (n=124)
Age; years	54,12 (SD 16,6)	54,36 (SD 17,29)	55,5 (SD 15.46)
ASA-PS			

I	1932 (15,8%)	285 (10,1%)	4 (3,2%)
II	6598 (54,1%)	1309 (46,5%)	17 (13,7%)
III	3186 (26,1%)	993 (35,3%)	69 (55,6%)
IV	433 (3,5%)	194 (6,9%)	31 (25%)
V	58 (0,5%)	35 (1,2%)	3 (2,4%)
Risk of death (Ex-Care model)			
Predicted mortality < 2%	9290 (76,1%)	1781 (63,2%)	48 (38,7%)
Predicted mortality 2-5%	1578 (12,9%)	490 (17,4%)	18 (14,5%)
Predicted mortality 5,0-9,9%	584 (4,8%)	223 (7,9%)	27 (21,8%)
Predicted mortality > 10%	755 (6,2%)	322 (11,4%)	31 (25%)
Surgical specialities			
General surgery	4417 (36,2%)	1076 (38,2%)	24 (19,4%)
Vascular	1356 (11,1%)	410 (14,6%)	17 (13,7%)
Thoracic	296 (2,4%)	113 (4%)	38 (30,6%)
Orthopedics	1095 (9%)	226 (8%)	6 (4,8%)
Urology	2094 (17,2%)	463 (16,4%)	13 (10,5%)
Neurosurgery	374 (3,1%)	159 (5,6%)	8 (6,5%)
Others**	2575 (21,1%)	369 (13,1%)	18 (14,5%)
Major Surgery	3058 (25,1%)	957 (34%)	38 (30,6%)
Urgent Surgery	2473 (20,3%)	996 (35,4%)	46 (37,1%)
In-hospital death	309/12207 (2,5%)	180/2816 (6,4%)	32/124 (25,8%)

** breast, head & neck, gynecology, and plastics as others

We observed a significant increase in in-hospital deaths within 30 days after surgery during pandemic. The mortality rate was 2.5% (309/12207) in the control group versus 7.2% (212/2949) during pandemic cohort (COVID positive and negative). COVID positive patients had mortality of 25.8% (32/124) and COVID negative patients of 6.4% (180 /2816) during the same period. We also identified an increase of 100% in mortality in intermediate and high-risk classes and 75% of increase in mortality in low-risk negative COVID patients operated during pandemic.

Unadjusted relative risk of pandemic group effect was 2,84 (95% IC 2.40-3,37)]. After adjustment for basal risk of mortality compounded by Ex-care risk model (age, ASA, severity of procedure and urgency), presence of COVID infection and surgical specialties the effect of being operated during pandemic (effect of group) remained significant, with an adjusted RR

of 1,52 (95% CI 1.27-1.84). See Table 2 for detailed model. We also found independent associations between mortality and Ex-care risk categories, COVID infection [RR 1.76 (95% CI 1.19-2.60)] and thoracic specialty [RR 2.03 (95% CI 1.51-2.72)].

We calculated a post-hoc power of 99.6% for this result, considering all variables on Table 2, including 15.147 subjects (2949 in the pandemic group), adjusted for its variables, including surgical specialties, considering 5% significance.

Table 2; Unadjusted and adjusted association between pandemic group and in-hospital mortality in 15.147 patients according to Ex-care classes (includes age, ASA, surgical nature and severity)

RR (IC95%)		P value
UNADJUSTED MODEL (n = 15147)		
Pandemic group	2,84 (2.40-3,37)	< 0,001
ADJUSTED MODEL (n = 15147)		
Pandemic Group	1,52 (1.27-1.84)	< 0,001
COVID Positive	1.76 (1.19-2.60)	< 0,004
Ex-Care Risk classes		
Ref Predicted mortality < 2%	Ref (0)	
Predicted mortality ≥10%	39.14(29.14-52.57)	< 0,001
Predicted mortality 5,0-9,9%	13.64(9.58-19.43)	< 0,001
Predicted mortality 2-5%	7.26(5.12-10.24)	< 0,001
Surgical specialties		
General Surgery	Ref (0)	
Vascular	0.68(0.54-0.87)	0.02
Thoracic	2.03(1.51-2.72)	<0.01
Orthopedics	0.62(0.39-0.68)	0,42
Urology	0.48 (0.33-0.68)	<0.01
Neurosurgery	1.75(0.89-1.54)	0,25
Others**	0.43 (0.26-0.7)	0,01

DISCUSSION

The COVID pandemic has displaced many other health system priorities, with a strong negative impact on the treatment of many diseases. The main finding of this study was that postoperative mortality was substantially increased among patients submitted to surgery during pandemic, with or without COVID infection, in a university hospital in a LMIC context. We find out that being operated during pandemic, was associated with an increased risk of 52% of dying in the postoperative period. This negative effect of pandemic was demonstrated in a multivariable model controlled for the main clinical and surgical risk variables.

The disruption of drug and equipment supply chain, interruption of therapies, shortness and reassignment of staff, or postponing detection of new cases produce excess of morbidity and mortality linked to other diseases. This situation is of significant concern in places that work already with the limits of the resources and inequity. These inequality resourced health systems have hampered the response to the pandemic in all Latin America. As a continent, South America constitutes 18.4% of the cumulative confirmed deaths from COVID19¹².

In Brazil, the health-system preparedness was decentralized and varied a lot through regions⁴. The side effects of pandemic in health assistance were expected but need to be understood. This pragmatic study cannot address all important questions, but will help to identify where the problems related to surgical assistance are.

Multiple processes underpinned the worst outcomes in surgical care in our institution. Firstly, throughout the pandemic, elective surgical procedures were kept as minimum and surgical movement reduced to one third, while the hospital's ICU capacity increased 217%. Surgical patients have experienced delays in their treatments and consultations and those with the advanced condition of disease and non-elective cases compounded the surgical agenda during peak months. Second, the hospital rapidly increased the number of COVID-19 dedicated professionals and opened new clinical ICU Units and wards to attend a 4 million population region. Surgical wards became COVID units and the surgical human resources were displaced to attend to this new demand. Anaesthesia machines were converted to respiratory support units and postoperative recovery rooms were converted to intensive care to manage COVID sick patients. Third, the unprecedented demand for ICU beds leads to the reduced threshold for high-risk surgical patients discharge from ICU or recovery units to common wards, where assistance was hampered by the high turnover of employees. Finally, ward surgical pathways were discontinued, such as the co-management for hip fracture, the pathway dedicated to high-risk surgical patients, or enhanced recovery program. The displacement of physiotherapists and rescue clinical team led to the suboptimal postoperative care for these vulnerable groups. In summary, there was a real threat of disruption to all surgical services and even critical surgical care was harmed.

When we compare our data to the present literature, we found similar results of significant increase in mortality rates in COVID positive patients. In single center study in Italy, it was found 19,5% of postoperative mortality in COVID positive patients and 2,44% in non-covid patients⁷. In a multicentric study with 1128 patients operated with pre or postoperative diagnosis of COVID the 30-day mortality was 23,8%¹³. The same research group found out in a cohort of 140.231 patients operated during pandemic an adjusted 30-day mortality rate in those who did not have SARS-CoV-2 infection of 1.5% (95%CI 1.4–1.5). The mortality was increased in patients who had surgery at 0–2 weeks, 3–4 weeks and at 5–6 weeks after SARS-CoV-2 diagnosis (odds ratio (95%CI) 4.1% (3.3–4.8), 3.9% (2.6–5.1) and 3.6% (2.0–5.2), respectively). This study ground the current guideline to postpone elective surgeries at a minimum of 6-week after COVID infection¹⁴. Our mortality rate in COVID patients (25%) was similar to these previous studies, otherwise the 6,4% mortality in non-COVID general patients (180/2816) was higher than any other report of postoperative mortality in large international cohorts in different continents¹⁵⁻¹⁷. Also, it represents a substantial increase of 156% in mortality rates, in relation to the two previous years at the same hospital. This excess of mortality occurred in all risk classes and cannot be attributed exclusively to patients and surgical factors (Figure 3). Even considering differences in the case-mix between the control and pandemic cohort, all classes of risk patients had disproportionately high mortality incidence.

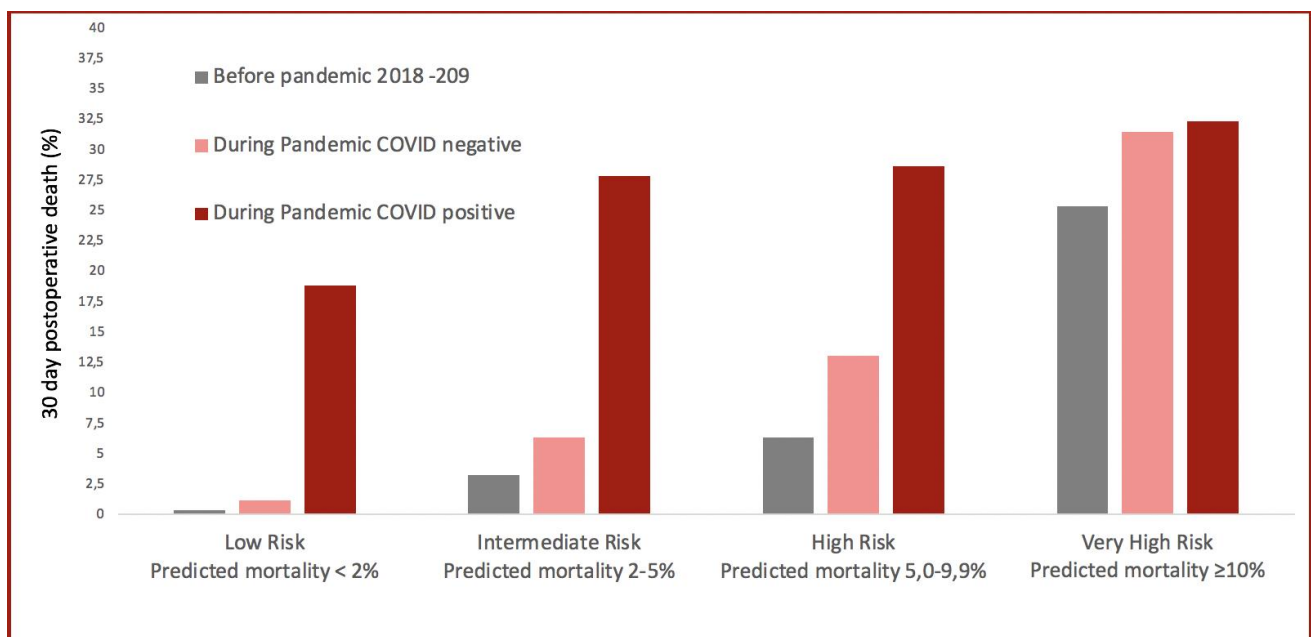
The strengths of this study include the great number of patients evaluated before and after cohort. As far as we know, this is the first study that searched for the “pandemic effect” on health surgical processes and surgical mortality in patients without COVID infection in a LMIC scenario. Being a single center study with a tightly matched control population allows the evaluation of the impact of pandemic in changing assistance processes. We used a validated risk stratification tool, developed for Brazilian population assisted in public health system, the Ex-Care risk model⁹, to standardise risk assessment of death for individual patients. The Ex-care risk model result is an index compounded by clinical (ASA physical status and age) and surgical (nature and severity) characteristics that made possible the precise comparison of patient’s in different cohorts.

Our study has several limitations. Firstly, it is vulnerable to bias regarding its cohort design nature. However, the before-and-after design has a pragmatic approach, therefore it is able to capture relevant outcomes using an appropriate comparison group¹⁸. Second, its results may not reflect the Brazilian or LMIC reality, since it is a single-centre study in a country with profound inequalities in health assistance. Third, ascertainment of SARS-CoV-2 status was based on routine pre-operative tests, therefore, it is possible that some patients

have been misclassified. Finally, we evaluated in-hospital mortality without evaluating long-term mortality, complications or other patient-centered outcomes.

The COVID-19 pandemic has led to the disruption of routine surgical services. We described the immediate impact on patients' outcomes during the pandemic in a referral hospital in Brazil. Wide inequalities in the Health system determined the disproportionate burden on our hospital, in spite of the availability of health care resources and structure. Although lesser lethal variants are circulating, the pandemic is not overcome. It exacerbated health disparities and will leave a significant residual impact on the surgical system. This episode in global health has reinforced the need to adopt strategies to strengthen surgical systems to save lives and promote economic growth in LMIC.

Figure 3. Relationship between Ex-Care risk and mortality



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