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Neurosurgical patients' morbidity and mortality during the COVID-19 pandemic: An integrated review

Morbidade e mortalidade de pacientes neurocirúrgicos durante a pandemia de COVID-19: Uma revisão integrada

Morbididad y mortalidad de pacientes neurocirúrgicos durante la pandemia COVID-19: Una revisión integrada

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Abstract
Objective: To assess mortality among neurosurgical patients during the COVID-19 pandemic period. Methods: This study entails an integrative literature review conducted by querying predefined descriptors in databases including Science Direct, PubMed®, and the Biblioteca virtual em saúde. Results: A total of 777 articles were identified. After applying inclusion and exclusion criteria, 14 studies were selected to constitute the foundation of this review. A disparity emerged across studies concerning alterations in mortality rates during the COVID-19 pandemic. While the majority of articles (n = 6) reported an increase in mortality, four studies observed no change in mortality rates when comparing the pandemic period with the pre/post-pandemic period. Regarding the number of neurosurgical procedures, a variable decline was observed across studies, ranging between 11.5% and 43%. The majority of articles documented a rise in postoperative complications during the pandemic. Conclusion: A significant impact of the SARS-CoV-2 pandemic on the surgical context was observed, as there was a notable reduction in the number of surgeries performed, leading to an increase in postoperative complications and potentially the mortality rate.
Keywords: COVID-19; Neurosurgery; Period, postoperative; SARS-CoV-2.

Resumo
Objetivo: Avaliar a mortalidade entre pacientes neurocirúrgicos durante o período de pandemia de COVID-19. Métodos: Este estudo consiste em uma revisão integrativa da literatura realizada por meio de consulta a descritores pré-definidos em bases de dados como Science Direct, PubMed® e Biblioteca virtual em saúde. Resultados: Foram identificados 777 artigos. Após aplicação dos critérios de inclusão e exclusão, foram selecionados 14 estudos para constituir a base desta revisão. Surgiu uma disparidade entre os estudos sobre alterações nas taxas de mortalidade durante a pandemia de COVID-19. Embora a maioria dos artigos (n = 6) tenha relatado aumento na mortalidade, quatro estudos não observaram alteração nas taxas de mortalidade ao comparar o período pandêmico com o período pré/pós-pandemia. Em relação ao número de procedimentos neurocirúrgicos, foi observado declínio variável entre os estudos, variando entre 11,5% e 43%. A maioria dos artigos documentou um aumento nas complicações pós-operatórias durante a pandemia. Conclusão: Observou-se um impacto significativo da pandemia SARS-CoV-2 no contexto cirúrgico, pois houve uma redução notável no número de cirurgias realizadas, levando a um aumento das complicações pós-operatórias e potencialmente da taxa de mortalidade.
Palavras-chave: COVID-19; Neurocirurgia; Período pós-operatório; SARS-CoV-2.

Resumen
Objetivo: Evaluar la mortalidad entre pacientes neuroquirúrgicos durante el período de la pandemia de COVID-19. Métodos: Este estudio implica una revisión integradora de la literatura realizada mediante la consulta de descriptores predefinidos en bases de datos que incluyen Science Direct, PubMed® y la Biblioteca virtual em saúde. Resultados: Se identificaron un total de 777 artículos. Luego de aplicar criterios de inclusión y exclusión, se seleccionaron 14 estudios para constituir la base de esta revisión. Surgió una disparidad entre los estudios sobre las alteraciones en las tasas de mortalidad durante la pandemia de COVID-19. Si bien la mayoría de los artículos (n = 6) informaron un aumento en la mortalidad, cuatro estudios no observaron cambios en las tasas de mortalidad al comparar el período

pandémico con el período pre/pospandémico. En cuanto al número de procedimientos neuroquirúrgicos, se observó una disminución variable entre los estudios, que oscila entre el 11,5% y el 43%. La mayoría de los artículos documentaron un aumento de las complicaciones posoperatorias durante la pandemia. Conclusión: Se observó un impacto significativo de la pandemia SARS-CoV-2 en el contexto quirúrgico, ya que hubo una reducción notable en el número de cirugías realizadas, lo que llevó a un aumento de las complicaciones postoperatorias y potencialmente de la tasa de mortalidad.
Palabras clave: COVID-19; Neurocirugía; Período postoperatorio; SARS-CoV-2.

1. Introduction

Infection by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is responsible for Coronavirus Disease 2019 (COVID-19), which has resulted in an increasing number of cases worldwide. In February 2020, the World Health Organization declared the COVID-19 pandemic. The infection with SARS-CoV-2 manifests across a broad clinical spectrum, ranging from asymptomatic and mild symptomatic cases to severe cases requiring Intensive Care Unit (ICU) support. In response, interventions were implemented to reduce SARS-CoV-2 transmission, primarily through droplet and aerosolized secretion inhalation (Smith, 2023; Mallah et al., 2021; McIntosh, 2023).

Among the measures taken to control SARS-CoV-2 transmission, adjustments in healthcare services were made, including the reduction of elective surgeries and hospital stays, suspension of most outpatient services, and other measures aimed at ensuring patient safety and preventing institutional collapse. Notably, oncology patients were given priority for surgical interventions. However, in cases requiring intensive postoperative care, challenges arose, particularly for neuro-oncological surgical patients who predominantly require ICU beds (Spinelli & Pellino, 2020; Santi et al., 2021; Hameed et al., 2021).

Throughout the SARS-CoV-2 pandemic, emergency surgical units were maintained, performing procedures regardless of positive or negative COVID-19 testing results (Spinelli & Pellino, 2020; Santi et al., 2021). It is noteworthy that despite the continuity of urgent and emergency services, due to reduced staff and equipment availability, there were instances of delayed urgent surgeries, leading to an increased risk of complications (Vanni et al., 2020). In addition to implementing COVID-19 transmission reduction protocols in healthcare settings, triage strategies were employed to optimize waiting times for surgical procedures in some institutions (Bouthillier et al., 2021).

Immediate neurosurgical treatment for central nervous system tumors, whether benign with significant mass effect or malignant, is essential for patient prognosis. However, during the SARS-CoV-2 pandemic, along with a decrease in the number of neurosurgical procedures performed, evaluating whether the immediate surgical intervention's benefits outweighed the risk to patients and healthcare professionals from the coronavirus became necessary. Consequently, guidelines were developed during the pandemic to guide patient management and prioritize cases (Amoo et al., 2021; COVIDSurg Collaborative, 2020; Zoia et al., 2020).

In light of the above, this study aims to assess the mortality rate among neurosurgical patients during the SARS-CoV-2 pandemic in comparison to the pre- and post-pandemic periods.

2. Methodology

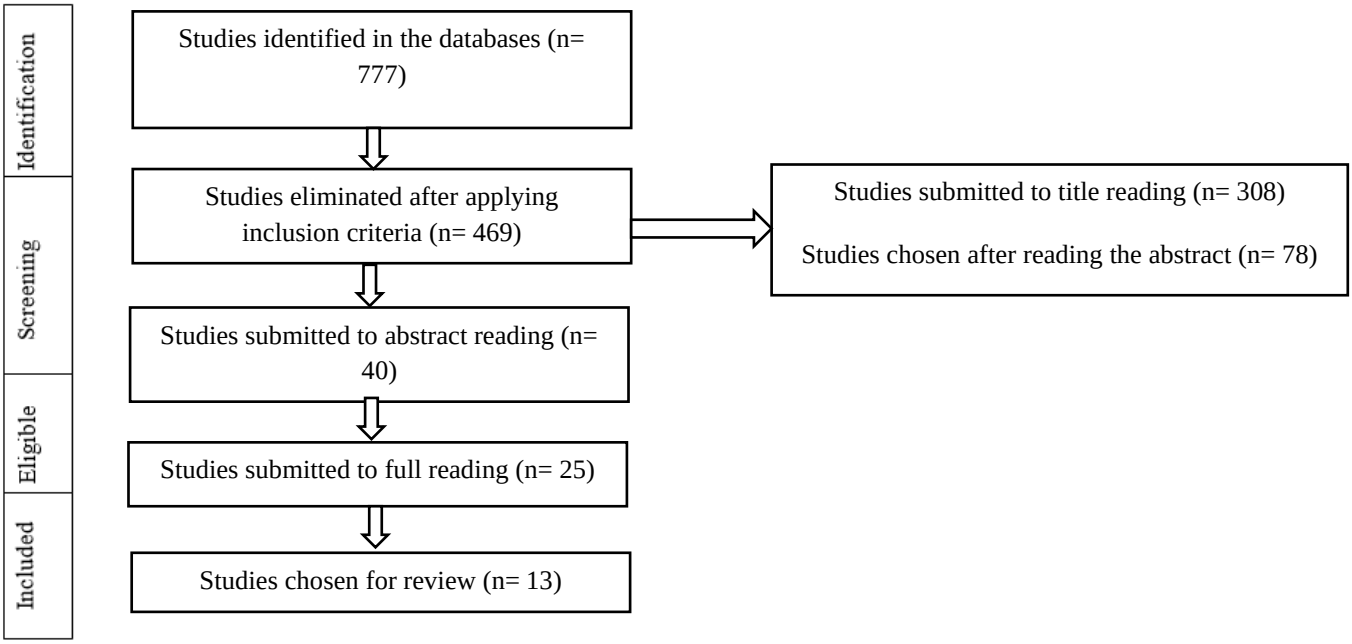
This is an integrative review aimed at synthesizing knowledge on a specific topic by incorporating results from significant studies. In this case, the objective is to evaluate the mortality rate in neurosurgical patients during the SARS-CoV-2 pandemic. To achieve this, six steps are followed: identifying a thematic question to guide the review, establishing descriptors and inclusion/exclusion criteria for articles based on this question, defining the sampling strategy and information to be extracted from the reviewed studies, and finally, conducting an analysis and discussion of the results, which are synthesized and presented in the review (Souza et al., 2010).

In this review, the guiding question was, "Was there an increase in mortality during the pandemic in neurosurgical patients?" To answer this question, databases such as PubMed®, the Virtual Health Library (BVS), and ScienceDirect were utilized. A search was conducted using the descriptors "COVID-19" (D1), "SARS-CoV-2" (D2), "Postoperative Period" (D3), and "Neurosurgery" (D4), employing the Boolean operator "AND" to enhance results. This was combined as "D1" AND "D3" AND "D4," and "D2" AND "D3" AND "D4."

The inclusion criteria were articles available in full and openly accessible, with no language or publication year restrictions. Studies lacking sufficient data to fulfill the review's objective or discussing a different theme were excluded. Initially, 777 studies were identified in the databases. After applying the inclusion criteria, 308 articles remained for title review, from which 78 were selected for abstract review. Subsequently, 38 duplicates were excluded, leaving 40 abstracts for review, of which only 25 were subjected to full-text reading. Among these, 13 studies were chosen to be included in this review's database, with only 1 of them being a meta-analysis (Figure 1).

The results of these studies were carefully interpreted, involving a meticulous comparison between their outcomes and conclusions.

Figure 1 - Process carried out to select articles.



Source: Study data (2023).

3. Results

A total of 81,531 neurosurgical procedures in patients were evaluated during the pandemic period or the pre/post-pandemic period. The United States was the location with the highest number of studies, accounting for approximately 23% (n = 3) of the total articles, followed by Egypt with around 15.4% (n = 2). Only 1 selected study was published in a journal without impact factor (Table 1).

Table 1 - Characteristics of studies selected for review.

Author	**Journal (Impact factor)**	**Location**	**Neurosurgery**	**Sample (N)**	**Mean age**	**Type of study**
Amoo at al., 2020	Irish Journal of Medical Science (2.089)	Ireland	Neuro-oncology (glial and non-glial tumors)	175 (127 patients in 2020 and 139 in 2019)	Average 52.7 years in 2020 and 52.2 in 2019	Retrospective
Tavanaei et al., 2021	World Neurosurgery (2.21)	Will	Elective and emergency	816 procedures (533 pre-COVID-19 and 283 COVID-19)	Average 48.07 years in 2020 and 49.58 in 2019	Case-control
Noureldine et al., 2020	World Neurosurgery (2.21)	Florida (USA)	Emergency / Urgency	305 (91 patients in COVID-19 and 214 in regular period)	Average 52.9 years	Prospective
Hernández et al., 2023	Antibiotics (5.222)	Mexico	Neurosurgical procedure	4,150 procedures	-	Retrospective
Prasad et al., 2022	The American Journal of Surgery (2.403)	USA	Elective	60,853 patients	Median 67 years old3	Prospective multicenter
Lee et al., 2022	Korean Journal of Neurotrauma (0.56)	South Korea	Cerebral hemorrhage	143 patients	Control group 55.34 years and screening 59.96	Prospective
Singh et al., 2021	The Cureus Journal of Medical Science (1.2)	India	Elective	262 procedures	Median 52.5 years	Retrospective
Iglesias et al., 2021	Revista Argentina de Neurocirugía (0.08)	Argentina	Elective and emergency	434 procedures	-	Observational retrospective
Mallari et al., 2021	PLoS One (3.752)	California (USA)	Elective	295 patients (132 during and 162 pre-pandemic)	Average 53.2 pre-pandemic and 52.3 during	Retrospective
Azab & Azzam, 2021	Brain Disorders	Egypt	Gliomas	951 patients	-	Meta-analysis
Zanin et al., 2023	World Neurosurgery (2.21)	Italy	Neuro-oncology	11,443 (5,372 in the pandemic and 6,071 in the pre-pandemic)	-	Multicentric
Azab et al., 2021	Interdisciplinary Neurosurgery (0.182)	Egypt	Neurosurgical procedure	604 (300 in the pandemic and 304 in the pre-pandemic)	Average 50 pre-pandemic and 48 during	Unicentric cohort
Sá et al., 2021	Brazilian Journal of Anesthesiology (1.3)	Portugal	Emergency / Urgency	1,100 (457 patients in 2020 and 643 in 2019)	Median 67 years old in 2020 and 63 in 2019	Retrospective and observational

Source: Study data (2023).

Regarding mortality during the SARS-CoV-2 pandemic, it was observed that the majority of studies (n = 6; 46.1%) reported an increase in the mortality rate compared to the non-pandemic period. However, it's worth noting that the number of articles (n = 4; 30.8%) that did not observe a change in the rate was close to those that reported an increase. Only Amoo et al. (2020) reported a reduction in mortality during the pandemic, and Zanin et al. (2023) stated they couldn't definitively determine whether there was a change in the mortality rate or not (Table 2).

Table 2 - Summary of the results and conclusions of the selected articles.

Author	Key Findings	Conclusions
Amoo et al., 2020	There was no increase in the average time from referral to inter-hospital transfer or from admission to surgery in acute hospitalizations. The 30-day postoperative morbidity and mortality rates were lower in 2020, at 8.7% (n = 11), compared to 2019, at 10.1% (n = 14), both as a result of rapid tumor progression. There was 1 death related to COVID-19.	The postoperative morbidity and mortality rates were lower in 2020. However, neuro-oncological surgery can be safely continued during pandemics if a rigorous testing framework is implemented.
Tavanaei et al., 2021	There was a significant reduction in the number of procedures during the pandemic (n = 533 vs. n = 283), with a decrease in elective admissions and an increase in emergency admissions. Neurosurgical causes remained unchanged during the pandemic when analyzing proportional distribution. General mortality was comparable between the pre-COVID-19 and COVID-19 periods, but patients concurrently infected with SARS-CoV-2 had substantially higher mortality (65%).	Comparable overall mortality between the pre-COVID-19 and COVID-19 periods was observed. Adequate implementation of safety and screening protocols allows for the maintenance of emergency care with a reduced risk of SARS-CoV-2 hospital-acquired infection, its complications, and mortality in neurosurgical patients during the pandemic..
Noureldine et al., 2020	The mortality rate was 7.7% (n = 7) in patients assessed over a 4-week period during the COVID-19 pandemic after protocol implementation, which is notably high and likely attributed to the shift from regular practice involving elective and emergency cases to exclusively emergency practice during the pandemic. When evaluating the control group undergoing procedures during regular practice, a change in the pattern of the most performed procedures is observed.	The implementation of properly executed protocols impacts the number and variety of neurosurgical cases but is pivotal. An increase in mortality rate during the pandemic is evident, likely a consequence of the emergency procedure profile.
Hernández et al., 2023	In 2020, the number of surgeries was reduced by 36% compared to 2019, while the rate of neurosurgical infections increased from 3.5% in 2019 to 5.6% in 2020. No significant differences were found in in-hospital mortality between the pre-pandemic year and the three pandemic years, nor in antibiotic resistance patterns.	There was a significant impact in the first year of the COVID-19 pandemic, evident in the reduced number of surgeries and increased postoperative infections. Restricted hospital access affected seriously ill patients' access to medical care, increasing the risk of complications and mortality. However, this study did not show a significant alteration in the mortality rate.
Prasad et al., 2022	The risk of COVID-19 infection within 30 days postoperatively is elevated in patients with a high number of comorbidities and those undergoing neurosurgical procedures, necessitating closer postoperative monitoring. A positive test in the postoperative period is significantly associated with a higher risk of complications, including mortality. Groups that remained negative or tested positive prior to surgery did not exhibit differences in outcome rates.	PCR screening minimized postoperative COVID-19 infection and its complications in the majority of elective cases. The group that tested positive within 30 days postoperatively had a higher rate of severe complications (mortality, readmission, reoperation), pulmonary complications, other complications, and longer hospital stays compared to those who remained negative or tested negative.
Lee et al., 2022	There were no significant differences in the time to surgical intervention, prognostic assessment scores, and mortality among patients with cerebral hemorrhage who underwent COVID-19 screening tests and the control group. Despite the pandemic affecting neurosurgical treatment due to the cancellation of elective surgeries and reduction in outpatient services.	There was no significant change in patient treatment and prognosis, including mortality, due to additional time required for pre-operative screening tests during the pandemic.
Singh et al., 2021	Among 262 non-elective neurosurgical procedures, there were 10 COVID-19-positive patients undergoing surgery, accounting for 3.8% of the interventions, of whom one progressed to mortality within a 30-day postoperative period. Mortality increases with advancing age and a higher number of comorbidities. Similarly, symptomatic cases with postoperative pulmonary complications exhibit a higher mortality rate compared to those without such complications.	Postoperative outcomes were favorable in COVID-19-positive patients, suggesting that neurosurgical interventions in these cases should be comparable to non-COVID-19 cases. Some modifications are associated with preventing the spread of infection among healthcare professionals.
Iglesias et al., 2021	There was a 43% decrease in the total number of surgeries in 2020 compared to 2019. Significant differences were observed between the groups in postoperative clinical complications (13.09% vs 32.29%) and hospitalization. Higher mortality rates were noted during the pandemic period.	There was a significant increase in clinical complications, postoperative hospital mortality rate, and the number of hospitalization days, with no significant differences in functional status at discharge during the pandemic.
Mallari et al., 2021	There was a reduction in the use of ICU from pre-pandemic to pandemic, from 92 (54%) to 43 (29%) of the surgeries ($p<0.001$), as well as in the length of hospital stay. There were no differences in mortality rates or rates of resection/remission, readmissions, or reoperations within 30 days.	The protocol developed during the COVID-19 pandemic led to a safe reduction in the use of ICU and hospital stay days without an increase in complications, mortality, readmissions, or reoperations.

Azab & Azzam, 2021	Eight studies were included in the meta-analysis, comprising a sample of 951 patients with glioma, of which 74 progressed to death and 250 experienced complications, both surgical and non-surgical in nature.	Overall complications and mortality were more significant among COVID-19-negative patients. The number of surgical admissions did not significantly differ between COVID-19-negative and positive cases.
Zanin et al., 2023	There was a decrease of 699 operated neuro-oncology patients when comparing the pre-COVID-19 period to the COVID-19 period. There was a slight increase in emergency surgeries and a marked decline in benign and elective pathologies during the COVID-19 period. However, none of these differences were statistically significant. There were 36 cases positive for SARS-CoV-2, of which 11 resulted in death, with only 2 cases having COVID-19-related deaths. It is impossible to determine whether mortality from neurosurgical disease increased during COVID-19.	There was a reorganization of Italian neurosurgical departments during the pandemic to enable the treatment of CNS tumors without compromising surgical efficacy and safety. There was a decrease in procedures due to the geographic redistribution of disease management and resource reduction. This decrease was not statistically significant. Further studies are needed to investigate whether this corresponds to an increase in mortality..
Azab et al., 2021	There was a higher mortality outcome in neurosurgical interventions during the pandemic, but there was no significant difference in the average length of hospital stay. However, the anesthesia time was prolonged while the operation time was reduced.	The mortality outcome of neurosurgical procedures was higher during the pandemic.
Sá et al., 2021	There was a reduction of approximately 30% in urgent/emergency neurosurgeries during the pandemic, with no difference in the waiting time for surgery. Additionally, there was higher mortality among patients who underwent surgery during the 2020 pandemic compared to that of 2019, from 11.4% to 5.9%.	The COVID-19 pandemic led to a decrease in urgent/emergency neurosurgeries. A pre-operative screening strategy was implemented without compromising the efficiency of services. Despite similar characteristics, there was higher mortality during the pandemic.

Source: Study data (2023).

Postoperative complications were assessed in 5 selected articles (38.5%) for this review, with 4 articles (30.8%) reporting an increase in the number of complications during the pandemic. Regarding the number of neurosurgical procedures performed, a significant decrease was observed during the COVID-19 pandemic, as mentioned in 7 studies (53.8%). This reduction varied between 11.5% and 43% (Table 2).

4. Discussion

The analysis of the impact of the COVID-19 pandemic on the mortality of neurosurgical patients reveals significant findings. A portion of the studies (30.8%) demonstrated no significant alteration in mortality rates when evaluating the pandemic and pre/post-pandemic periods. However, the majority of studies included in this review concluded that there was an increase in mortality during the COVID-19 pandemic compared to the pre/post-pandemic period.

Pert et al. (2022) conducted a comprehensive analysis of 5,077 non-elective emergency neurosurgical cases across various centers in Austria and the Czech Republic from 2017 to 2021. Their findings indicated that the 30-day mortality rate exhibited no substantial alteration. Notably, despite the substantial prevalence of COVID-19 cases, there was no discernible deficit in intensive care capacity, even at the peak of the pandemic. This perception was consistent with the study conducted by Abduljawwad et al. (2023), who examined 722 spine surgeries, revealing similar mortality rates from 2.9-9.7% during non-pandemic phases to 6.2-11.3% amid the pandemic.

Amoo et al. (2020) do not observed higher postoperative mortality rates within 30 days in 2020 when compared to 2019. Similarly, Azab & Azzam (2021) concluded that general complications and mortality were not more significant among COVID-19-positive patients. It's important to note that Zanin et al. (2023) stated that they were unable to establish whether the mortality in neurosurgical patients increased during SARS-CoV-2 infection.

The studies that concluded there was an increase in mortality during the pandemic account for 46.1% of the articles (n = 6) of the articles. Macêdo Filho et al. (2021) evaluated neurosurgical procedures performed in Brazil from 2019 to 2020 using Brazilian Hospital Information System records, and found a 21.26% increase in in-hospital mortality rate. Karimov et al. (2023) analyzed 6 months of both 2019 and 2020 in a Turkish university hospital, encompassing a total of 1,767 neurosurgical

procedures. They reported a general increase in the mortality rate from 6.8% pre-pandemic to 9.6% during the pandemic (p = 0.03).

Concerning the rate of postoperative complications, the majority of studies in this review observed an increase in the number of cases. When assessing the rate of postoperative infections in neurosurgical procedures, Hernández et al. (2023) found an increase from 3.5% in 2019 to 5.6% in 2020. Jankovic et al. (2022) reported no reduction in the number of infections, despite prevention measures implemented during the pandemic. Some studies, however, did not observe an increase in the number of complications during the pandemic (Mallari et al. 2021). Similarly, Jankovic et al. (2022) studied postoperative complications in spine surgeries, analyzing 838 procedures during the non-pandemic period and 831 during the pandemic, with comparable complication rates between the group.

Patients with COVID-19 may face an increased risk of morbidity and mortality during the infectious period and for some time after recovery, regardless of the surgical procedure to be performed. The risk of perioperative morbidity and mortality may increase in COVID-19 patients even after recovery, especially concerning pulmonary complications and mortality after surgery performed up to seven to eight weeks after infection diagnosis (London, 2023; COVIDSurg Collaborative, 2020). Alongside the risk of healthcare worker contamination, the observation of higher morbimortality rates in COVID-19-infected patients led to the postponement of surgeries until recovery, except for urgent or emergent surgical procedures (London, 2023; Doglietto et al., 2020; Deng et al., 2022).

Examining the number of neurosurgical procedures conducted during the pandemic, the literature emphasizes a variable reduction in surgeries across seven studies. Sá et al. (2021) reported a decrease from 643 urgent/emergency neurosurgical procedures in 2019 to 457 in 2020, reflecting an approximate 30% reduction. In congruence, Hernández et al. (2023) and Tavanaei et al. (2021) documented reductions of around 36% and 35%, respectively. Within these studies, Hernández et al. (2023) evaluated 1,219 procedures in 2019 and 781 in 2020, while Tavanaei et al. (2021) compared 495 pre-pandemic cases to 321 during the pandemic in 2019.

Iglesias et al. (2021) highlighted a more substantial decline of approximately 43% in the total number of surgeries in 2020 (n = 275) compared to 2019 (n = 157). In contrast, Zanin et al. (2023) reported a more modest decrease of around 11.5%, encompassing 6,071 procedures conducted in the pre-COVID-19 period and 5,372 during the COVID-19 pandemic. When scrutinizing 11 neuro-oncological procedures in Brazil between 2019 and 2020, Macêdo Filho et al. (2021) found that there was a 21.5% reduction (n = 28,858 cases) in neurosurgical procedure volume. This reduction was particularly striking for elective procedures, showing a notable drop of 42.46%. Furthermore, Tavanaei et al. (2021) observed a decrease of 55.8% in elective procedures (n = 380 vs. n = 168). In a similar vein, analyzing 1,767 neurosurgical procedures, Karimov et al. (2023) found that 972 were in the pre-pandemic period and 795 were during the pandemic, leading to an 18.2% decrease. The prolonged deferral of neurosurgical procedures for specific indications was associated with increased morbidity and even mortality, as conditions progressed, resulting in neurological deterioration (Arimappamagan et al., 2021).

One notable limitation is the variability in the methodologies employed for outcome assessment across the included studies. This diversity in assessment methods could introduce heterogeneity in the data, potentially influencing the synthesis of findings. The absence of robust and uniform data prevents a more precise estimation of effect sizes. Furthermore, the reliance solely on available literature from specific databases may have led to the exclusion of relevant studies from other sources, thereby affecting the comprehensiveness of the review. Additionally, the quality of individual studies and the potential for bias within them are important factors to consider when interpreting the results.

5. Conclusion

A significant impact of the SARS-CoV-2 pandemic on the surgical context was observed, as there was a notable

reduction in the number of surgeries performed, leading to an increase in postoperative complications and potentially the mortality rate.

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