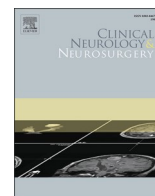




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Risk of contracting SARS-CoV-2 (COVID-19) from hospital admission and the impact of protection efforts on acute stroke treatment

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ABSTRACT

Background: It is unclear how interventions designed to restrict community and in-hospital exposure to the SARS-CoV-2 (COVID-19) virus influenced stroke care for patients seeking acute treatment. Therefore, we aimed to determine how these COVID-19 interventions impacted acute stroke treatment times and to assess the risk of contracting COVID-19 due to their stay in our medical center.

Methods: Retrospective, single center, two-phase study evaluating hospital and community trends from 12/2019 – 04/2020 compared to the previous year and pre/post (n = 156/93) intervention implementation. Phase I assessed stroke treatment times, delay to hospital arrival, and witnessed stroke volume. Phase II, a post-implementation telephone survey, assessed risk of developing symptoms or testing positive for COVID-19.

Results: Stroke volume declined by 29% (p < .05) from April to March compared to the previous year. However, no significant delays in seeking medical care (pre Mdn=112, post Mdn=95, p = .34) was observed. Witnessed stroke volume decreased 11% (p < .001) compared to the pre-implementation group, but no significant delay in IV alteplase (pre Mdn=22 mins; post Mdn=26 mins, p = .08) nor endovascular treatment (pre Mdn=60 mins; post Mdn=80 mins, p = .45) was observed. In Phase II, 63 patients participated, two tested (3%) COVID-19 positive during admission and four (6%) within two weeks of discharge. COVID-19 contraction risk during and after hospitalization remained similar to the general population (RR=1.75, 95%CI: 0.79–3.63). Overall results indicated a marked decrease in stroke volume, no significant delays to either seek or provide acute stroke care were evident, and COVID-19 contraction risk was low.

Conclusions: Seeking acute stroke medical care outweighs the risk of COVID-19 exposure.

1. Introduction

SARS-CoV-2 (COVID-19) manifests in most infected individuals as mild symptoms of dry cough, dyspnea, fever and in some cases may lead to severe complications such as pulmonary edema, sepsis, organ failure, pneumonia, and Acute Respiratory Distress Syndrome (ARDS) [1]. In addition, there has also been neurologic manifestations from COVID-19 with patients presenting with symptoms of nausea, headache, anosmia, ageusia, confusion, encephalitis, Guillain Barre syndrome and stroke [2]. The exact mechanism for these neurological presentations remain a reason for debate. The presentation of stroke among COVID-19 patients may be due to an increase of risk factors secondary to cardiotoxicity resulting from excess proinflammatory stimulation and transient hypercoagulability [2,3]. Stroke complications have also been reported after respiratory and urinary tract infections; mechanisms may include direct neurovascular involvement, inflammation (humoral or cellular), exacerbation of conventional stroke risk factors, or treatment related side effects [4,5]. Whether the risk of stroke associated with SARS-CoV-2 (COVID-19) infection is higher when compared to other infections remains to be proven.

The Center for Disease Control (CDC) and the World Health Organization (WHO) have helped to establish guidelines and recommendations for the community and healthcare settings with the aim to limit the transmission of COVID-19. As such, healthcare settings have been advised to minimize chances for exposures and implement measures before arrival, upon arrival, and for duration of visit until rooms are completely disinfected. Measures also included providing alternatives to face-to-face triage and visits [1,6]. During the initial stages of the US COVID-19 outbreak, Miami became the infection hot spot for the state of Florida. On March 1st 2020, the first Florida executive order went into effect declaring the COVID-19 pandemic as a public health emergency. By March 9th, the Emergency Operations Centers was activated to a level 2 and the stay-at-home order for Miami-Dade (MDC) and Broward counties went into effect. During this period, many of the local hospitals reduced the number of outpatient procedures, implemented COVID-19 screenings, promoted use of telehealth services, and limited visitors. Staff caring for patients suspected to have COVID-19 followed strict infection control measures including wearing facemasks, disposable gowns, eye protection, and frequent hand washing. As the quarantine and COVID-19 cases progressed, outpatient procedures were postponed,

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<https://doi.org/10.1016/j.clineneuro.2021.106793>

Received 3 March 2021; Received in revised form 24 June 2021; Accepted 26 June 2021

Available online 30 June 2021

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visitors, students, and volunteers were restricted from entering the hospital, and staff underwent daily symptom based screening and temperature checks before entering the hospital. In the community, people were instructed to stay home and only essential businesses such as pharmacies, grocery stores, and hospitals remained open with adjusted hours of operation. The community was encouraged to continue social distancing practices, to engage in hand hygiene, and to wear masks if entering essential businesses [1,6]. The COVID-19 pandemic has impacted the community in a variety of ways, including hospital admission rates; people are cautiously weighing the risks and benefits of being admitted to a hospital where COVID-19 patients are being treated. It is unclear how the interventions designed to restrict community and in-hospital exposure to COVID-19 affected the care for those stroke patients that sought treatment in our community. The objective of the following study is to determine the impact COVID-19 had on hospital stroke patient volumes, pre-hospital stroke transport, hospital arrival times and treatment times for patients evaluated as acute stroke alerts at the emergency room of Baptist Hospital of Miami (BHM). A co-primary objective of the study is to assess the risk of contracting SARS-CoV-2 from hospital admission, the suspected main reason why hospital visits have decreased.

2. Methods

This is a two-phase, single-centered retrospective study conducted at BHM in Miami, FL for patients admitted between December 2019 to April 2020. This study was reviewed and approved by the Baptist Health South Florida Institutional Review Board Committee (IRB #1603890). BHM is an 850-bed community hospital, serving a large Hispanic population with a certified comprehensive stroke center. Study population was composed of adults age 18 years or older presenting to the BHM emergency department (ED) as a stroke alert due to focal neurological symptoms compatible with acute stroke. Patients were excluded from the study if the stroke alert was made for patients already admitted to BHM (inpatient stroke alerts) or transferred from another institution.

Phase I of the study was a retrospective chart review to determine the impact of COVID-19 safety protocols on the management of an acute stroke. March 2nd 2020 marked the start date of SARS-CoV-2 safety protocols within BHM and was used as a cutoff to classify cases as “post” implementation group of SARS-CoV-2 safety protocols. Given that some changes were already occurring on a national level in February 2020, the dates from December 2019 through January 2020 were used as the “pre” implementation group for all further stroke treatment comparisons. The outcomes assessed in phase I included the time from symptom onset to hospital arrival (defined as the time witness or from detection of stroke symptoms if onset was unwitnessed), the percentage of stroke onset witnessed, mode of arrival, the total treatment time from symptom onset to intervention, door to CT scan, door to thrombolysis, door to groin time, door to reperfusion, the number of stroke admissions, the median NIHSS at baseline, length of stay, discharge destination, and SARS-CoV-2 status upon admission.

In phase II of the study, a telephone survey was conducted for the post implementation group to assess the risk of patients developing symptoms or testing positive for COVID-19 from hospital admission up to two weeks post discharge. The survey also assessed whether patients delayed their hospital arrival for the index stroke event due to concerns of contracting COVID-19.

Additional data was acquired for the assessment of stroke volume change and its relationship to COVID-19 prevalence. BHM stroke alert daily volume data for the previous year (February 2019 to April 2019) was acquired using the same inclusion and exclusion criteria outlined in the chart review. Additionally, daily admissions data for suspected and confirmed COVID-19 patients at BHM and MDC daily new COVID-19 cases between March 1, 2020 to April 30, 2020 were acquired.

2.1. Statistical analysis

The study sample was assessed for baseline characteristics such as age, race and sex. All data were assessed for normality and analyzed using SPSS v25 using a significant p-value of .05. Test statistics, central tendency, spread, effect size, and confidence interval are reported when appropriate. Mann Whitney-U tests were used to analyze differences between pre- and post-implementation groups for non-normal continuous variables; whereas Pearson chi-squared tests were used to analyze differences between categorical variables. Multinomial logistic regression was utilized to assess the influence of safety precaution implementation, arrival mode, if stroke symptom onset was known, time delays to seek medical attention, and stroke severity upon admission on disposition outcomes. To evaluate risk of contracting SARS-CoV-2, data regarding SARS-CoV-2 testing during phase I in the post implementation group was combined with the telephone survey data from phase II. Stroke alert volumes, BHM ED volumes, BHM COVID-19 admissions data, and MDC daily new cases data were consolidated by week. Using these data sets relative risk ratios were calculated to evaluate risk of contracting SARS-CoV-2 virus in stroke patients compared to the general population at BHM ED and MDC. Binomial logistic regression was used to assess factors that may have influence SARS-CoV-2 virus risk in stroke patients. Lastly, simple correlations and Pearson chi-square tests were used to assess the relationships between stroke alert volume and COVID-19 infection volumes.

3. Results

3.1. Volume and COVID-19

Comparisons between stroke alert volume data from Dec 2018-Apr 2019 to Dec 2019 to Apr 2020 revealed a year-to-year decline that was statistically significant ($\chi^2(21) = 40.57, p < .01$). No differences were detected from Dec to Feb ($\chi^2(12) = 15.25, p = .23$); however, from Mar to Apr there was 29% decline in stroke alert volume that was statistically significant ($\chi^2(8) = 16.18, p < .04$) (see Fig. 1). Correlational evaluations revealed a relevant negative relationship with a modest effect size that was not statistically significant between stroke alert volume and BHM COVID-19 reported cases ($r = -0.49, p = .09$). Unlike the BHM reported COVID-19 positive case volume, MDC COVID-19 reported cases were statistically significant ($r = -0.76, p < .05$). Correlational evaluation revealed a moderate negative relationship; as the number of reported positive COVID-19 cases in MDC increased there was a notable decrease in the volume of stroke alerts (see Fig. 2). Whereas, there was a statistically significant positive relationship with a moderate effect size between BHM ED total volume and stroke alert volume ($r = 0.70, p < .02$). As seen on Fig. 2, when BHM ED general volume decreased, so did the volume of stroke alerts.

3.2. Phase I

The study sample included 249 participants who were primarily Hispanic (65%, $n = 161$) females (57%, $n = 143$) with a median age of 75 (IQR: 62–83). As shown on Table 1, these characteristics did not statistically differ between the implementation groups (pre $n = 156$; post $n = 93$). There was a statistically significant change in the mode of arrival between the pre- and post-implementation group ($\chi^2(2) = 9.70, p < .01$). Relative to their sample size, EMS services were used 65% ($n = 101$) prior to the implementation of COVID-19 safety protocols and increased to 83% ($n = 77$) after implementation ($p = .07$). Whereas walk-in arrivals occurred 31% ($n = 48$) prior to implementation and decreased to 16% ($n = 15$) after implementation ($p < .001$). Furthermore, strokes alerts activated within the ED after patient arrival (ER Rescues), but prior to hospital admittance also decreased after implementation ($p < .03$). Similarly, the witness of stroke symptom onset showed statistically significant notable decline ($\chi^2(1) = 16.0, p < .001$).

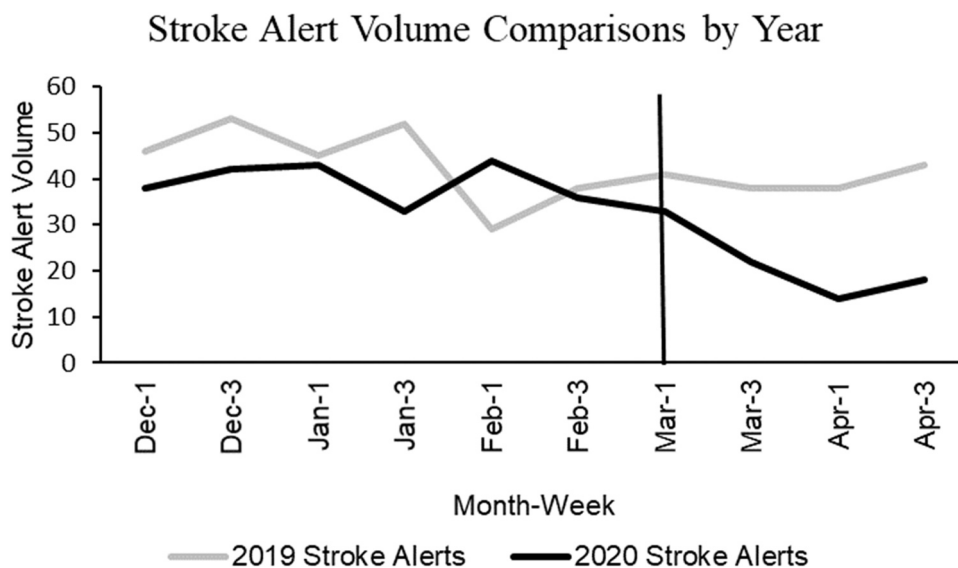


Fig. 1. Total stroke alerts by month and week number between Dec 2018 – Apr 2019 (gray) and Dec 2019 to Apr 2020 (black). The Black vertical line represents the week safety protocols for COVID-19 were implemented in the state of Florida.

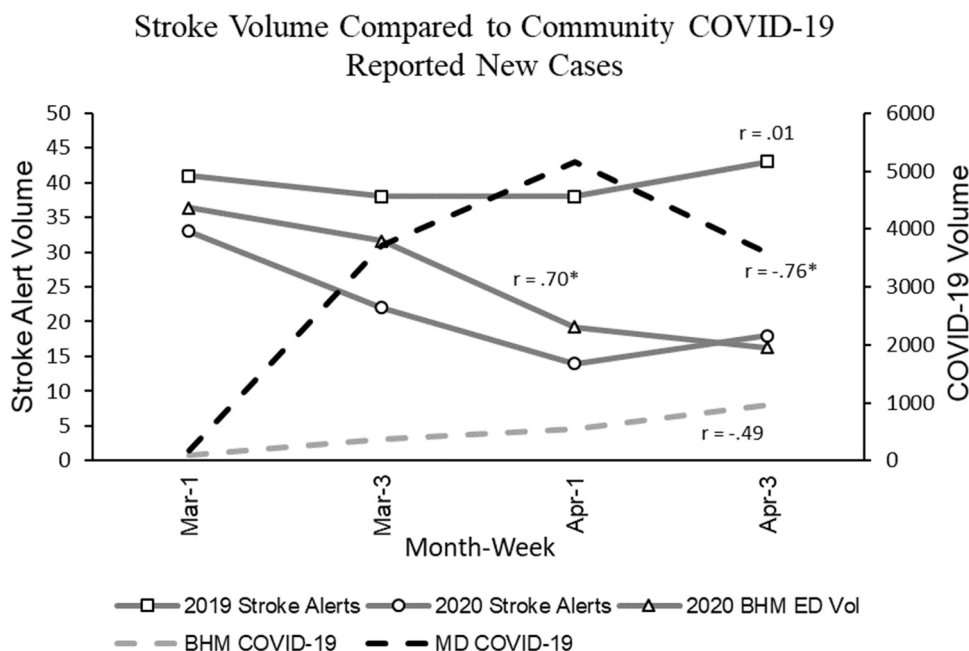


Fig. 2. This figure illustrates the correlational relationship between stroke alert volume in 2020 (open circles) to 2019 stroke alert volume (open squares), 2020 BHM ED volume (open triangles), BHM COVID-19 weekly new positive case volume (dashed light-gray), and Miami-Dade County weekly new positive case volume (dashed dark-gray). r = correlational value, $*p < .05$.

Prior to implementation, 64% (n = 96) of stroke symptoms were witnessed, whereas after implementation it declined to 53% (n = 48). Likewise, there was an increase in the number of patients with unknown onset (pre n = 1 (1%); post n = 6 (7%)); however, the percentage of patients with estimates of last known well remained similar (pre n = 53 (35%); post n = 36 (40%)). These changes in arrival mode and recognition of stroke symptom onset did not result in statistically significant delays in arrival to the ED ($z = -0.95, p = .34$), but there was a marked increase in stroke severity ($z = 2.01, p < .05$). Median delay to seek medical attention for the pre-group (n = 155) was 112 min (IQR 51–412) and the median delay for the post-group (n = 87) was 95 min (IQR 50–260). Delays could not be calculated for those with unknown symptom onset. Median NIHSS changes at admission were statistically

significant ($z = -1.97, p < .05$). For the pre-group (n = 156) the median NIHSS was 10 (IQR 7–21), while NIHSS for the post-group (n = 93) was 13 (IQR 7–17).

Stroke treatment volume and treatment times were compared between the pre- and post-implementation groups. A simple one-sample binomial test showed a significant decline in stroke volume in the post implementation as compared to the pre implementation group ($B(63,.5) = 7.8, p < .001$). In contrast there was a significant increase in the probability of patients receiving stroke treatment (i.e. thrombolytics, mechanical reperfusion, or both) ($\chi^2(1) = 4.66, p < .05$). Prior to implementation 15% (n = 23) of patients received stroke treatment, whereas, after implementation 26% (n = 24) of patients received treatment. Administration of IV alteplase, door to needle time, increased

Table 1
Clinical stroke alerts features pre & post implementation of COVID-19 safety protocols.

	Pre N = 156	Post N = 93	P-Value
Sample Characteristics			
Age, y, median (IQR)	73(61–83)	77(66–84)	.11
Female sex, n (%)	94 (60.3)	49 (53)	.24
Hispanic, n (%)	105(67)	56(60)	.31
Race			
Non-Hispanic White, n (%)	37(24)	22(24)	.87
Non-Hispanic Black, n (%)	11(7)	14(15)	.31
Stroke Alert Characteristics			
Mode of arrival			
EMS, n (%)	101(65)	77(83)	.07
Walk-in, n (%)	48(31)	15(16)	.001
ED Rescue, n (%)	7(5)	1(1)	.03
Witness Stroke Onset, n(%)	96(64)	48(53)	.001
Last known well, n (%)	53(35)	36(40)	.07
Unknown Onset, n(%)	1(0.7)	6(7)	.06
ED Arrival Latency, median (IQR) minutes	112 (51–412)	95 (50–260)	.34
Initial NIHSS score, median (IQR)	10(7–21)	13(7–17)	.05
Door to CT, median (IQR) minutes	10(7–20)	8(6–12)	.004
Treatment volume ¹ , n (%)	23 (15)	24(26)	.05
Door to Needle, median (IQR)	22(18–30)	26(22–45)	.08
Door to Groin, median (IQR)	60(50–91)	80(52–99)	.45
Discharge Disposition			
Home, n (%)	106(68)	57(62)	.001
Acute Inpatient Rehab, n (%)	20(13)	13(14)	.22
Long Term Care Facility, n (%)	16(10)	10(11)	.23
Hospice, n (%)	3(2)	4(4)	.71
Mortality, n (%)	10(6.5)	8(9)	.64

All values listed in bold were statistically significant. 1Patients treated with thrombolytics and/or endovascular thrombectomy.

from a median time of 22 mins (n = 16; IQR: 18–30) prior to implementation to 26 mins (n = 21; IQR: 22–45) after implementation. This increase was not statistically significant (z = 1.75, p = .08), but may be clinically relevant. Similarly, there were delays observed for endovascular treatment that were not statistically significant (z = 0.71; p = .45). Prior to implementation of COVID-19 safety measures the median door to groin time was 60 mins (n = 13, IQR: 50–91) and post implementation the median time was 80 mins (n = 12; IQR: 52–99). Surprisingly, there was a significant decrease in the latency to initial CT scan (door to CT time) after implementation (z = -2.8, p < .01). The pre implementation group median door to CT time was 10 mins (n = 155, IQR: 7–20); whereas the post implementation group median door to CT time was 8 mins (n = 93, IQR: 6–12).

When considering disposition outcomes prior to implementation, 68% (n = 106) were discharged home, 13% (n = 20) were discharged in an inpatient rehabilitation facility (IRF), 10% (n = 16) were discharged to a skilled nursing facility (SNF), and 8% (n = 13) were placed on hospice or expired. These percentages did not change significantly in the post implementation group, with the exception of discharge to home. There was a 6% decrease in the post implementation group compared to the pre-implementation group as shown in Table 1 ($\chi^2 = 14.73$, p < .001). However further analysis using multinomial regression ($R^2_{\text{nag}} = .47$, $\chi^2(33) = 119$, p < [0.001 revealed that pre or post SARS-CoV-2 (COVID-19) group, arrival mode, whether stroke symptom onset was known, or time delays to seek medical attention, did not significantly contribute to discharge placement. The only factor that did significantly change the odds of discharge placement was stroke severity at admission regardless of SARS-CoV-2 (COVID-19) group. A one unit increase in NIHSS at admission increased the odds of being discharged to an IRF or to a SNF by 15% (IRF: b=0.13, $\chi^2 = 8.15$, p < .01, B=1.15, 95% CI: 1.04 –1.26; SNF b=.14, $\chi^2 = 8.69$, p < [0.01 B=1.15, 95%CI: 1.05 –1.26) when compared to being discharged home. Higher NIHSS at admission increased the odds of being placed on hospice or expiring by 22% (b=0.20 $\chi^2 = 14.14$, p < .001, B=1.12, 95%CI: 1.10 –1.35) as

compared to being discharged home.

3.3. Phase II

A total of 92 participants from the post implementation group were contacted to participate in a survey. Of these, 20 were not reachable by phone and nine chose not to participate; the remaining 63 (69%) completed the survey (Supplemental figure). Only 4 (6%) of the 63 surveyed participants knowingly delayed seeking care due to concerns of contracting the virus.

Twenty-four participants out of the sixty-three (38%) were tested for COVID-19 during their hospital stay and thirty-two participants (51%) were tested in the 2-week period following their index stroke event (see Fig. 3a). Six participants (9%) reported testing positive for COVID-19. Two (3%) tested positive during their hospital stay and four (6%) tested positive in the 2-week period following their discharge (see Fig. 3b). Only three participants (5%) reported experiencing COVID-19 related symptoms; all three reported being COVID-19 positive. Admitted stroke patient risk of contracting COVID-19 was compared to the general BHM ED population (RR= 1.70, 95%CI: 0.79–3.63) and MDC new COVID-19 reported case rate (RR=.05, 95%CI: 0.02–0.11; both comparisons were not statistically different. Lastly, logistic regression analysis showed age, sex, ethnicity, admission NIHSS, mode of arrival, or stroke treatment type did not significantly influence COVID-19 risk during hospitalization or two weeks after discharge (see Supplemental table).

4. Discussion

This study provides further evidence of how the COVID-19 pandemic and the restrictions lowered the volume of stroke alerts compared to the previous year. This is consistent with other studies whose stroke admissions were also decreased secondary to the implementation of safety measures to aid in slowing the spread of COVID-19 [9–12]. The decrease in stroke alert volumes seems to be driven mostly by those with mild stroke symptoms as evidenced by a higher proportion of stroke admissions with increased stroke severity, an elevated IV alteplase and NIVR treatment rate, and an increase in the proportion of patients arriving via EMS. Other observations, including the increase in un-witnessed stroke onset, likely contribute to worsened patient outcomes as reflected by a

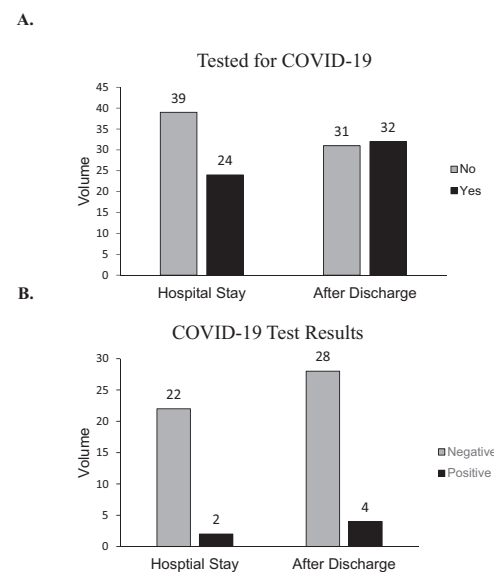


Fig. 3. The volume of patients who (A) received COVID-19 testing during their hospital stay or after discharge; (B) the number of patients surveyed who tested positive either during their hospital stay or after discharge.

decrease in patients being discharged directly home. Despite the additional challenges posed by the COVID-19 crisis we did not observe significant in-hospital treatment delays. Likely most differences in the stroke alerts characteristics reported in this analysis can be related to the impact of people being quarantined or remaining socially distant and the avoidance of medical treatment due to concern of contracting the virus within a hospital setting where COVID-19 positive patients are currently being treated.

To our knowledge, this is the first study assessing the risk of contracting COVID-19 during a stroke hospital admission and confirms other findings on the impact of safety protocols on the management of acute stroke during the height of the first COVID-19 infection surge in our community. At the peak of the crisis, the risk of contracting Covid-19 during, and within 2 weeks, from a stroke related hospital admission was at 9% of which only 5% reported COVID-19 symptoms (symptomatic COVID-19). The only other study looking at SARS-CoV-2 transmission within a hospital setting focused broadly on ED patients and likewise found visiting the ED was not associated with COVID-19 acquisition [7]. This may alleviate some concerns from patients in seeking medical care for stroke like symptoms. This risk is particularly low when compared to the known health effects of stroke. The cumulative all-cause mortality rate after stroke has been calculated to be 21.2% at 1 year and stroke is a leading cause of serious long-term disability in the United States [8]. Furthermore, we now have demonstrated effective treatment for acute ischemic stroke. None of the patients in this study were readmitted to our hospital system with severe COVID-19 infection.

Limitations of this study include its retrospective design and that it is single center. COVID-19 safety protocols and their impact on stroke care may vary between institutions and between different types of stroke center certification designations. Our analysis took place during the height of the first wave of the COVID-19 crisis for our community and therefore the risk of exposure would be expected to be less at later timepoints of the pandemic. Due to lack of community access to COVID-19 test results this study relied upon self-reported COVID-19 test recollection acquired during the phone interview. Also, during the analysis time period, testing was not yet widely available in the community, possibly underestimating exposure risk. Further not all participants were reachable by phone potentially affecting the generalizability of the results. However, in this analysis we mitigated these limitations by including symptom based screening and by looking at hospital readmissions. We included a 2-week period after hospital discharge as symptoms can take several days to develop. It is possible that some patients contracted COVID-19 after hospital discharge and be included in this report. This is however, also a strength, as it reflects the risk of contracting the infection not only during the acute care setting but also incorporates the immediate post-acute care. The analysis of the effects on treatment times may be limited due to low patient volumes.

5. Conclusion

This study demonstrates the risk of contracting COVID-19 during admission to the hospital for acute stroke care is comparable to that of the general community. It also confirms a decrease in stroke care volumes mostly by those with mild symptoms. Performance of in-hospital stroke care related metrics however can be largely maintained during the crisis as long as the hospital capacity is not overwhelmed. The benefits of seeking medical care for an acute stroke outweighs the risk of exposure to COVID-19.

CRedit authorship contribution statement

Jessica Greenwood, designed the data collection tool, collected and monitored data, drafted and revised the manuscript. Starlie Belnap, monitored data collection, wrote the statistical analysis plan, cleaned and analyzed data, drafted and revised the manuscript. Guilherme Dabus, reviewed and provided commentary for manuscript

improvement. Italo Linfante, reviewed and provided commentary for manuscript improvement. Felipe De Los Rios La Rosa, initiated collaboration, designed data collection tools, analyzed the data and revised the manuscript.

Funding statement

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests statement

Jessica Greenwood, none declared. Starlie Belnap, none declared. Guilherme Dabus, provides consulting and speaker support for the bureau of Medtronic, Microvention, Penumbra, and Cerenovus. Italo Linfante, serves as a consultant for Medtronic, Stryker, and Cerenovus. Italo Linfante also owns stake in InNeuroCo, Prometheus, and Prolong pharmaceuticals. Felipe De Los Rios La Rosa, none declared.

Acknowledgments

Special thanks to the Miami Neuroscience Data Team.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.clineuro.2021.106793](https://doi.org/10.1016/j.clineuro.2021.106793).

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