

EVALUATION OF OUTCOMES IN RURAL, NORTHERN, AND REMOTE PATIENTS TRANSFERRED TO A TERTIARY-CARE CENTRE IN MANITOBA DIAGNOSED WITH MODERATE TO SEVERE ACUTE PANCREATITIS: A RETROSPECTIVE STUDY

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Table of Contents

Acknowledgements	1
Introduction	2-3
Research Question and Objectives	3-4
Methodology	4-5
Study Design	4
Data Analysis	4-5
Ethics Approval	5
Results	5-8
Discussion	9-12
Study Limitations	12
Recommendations	12
Conclusion	12-13
References	13-14

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Introduction

Acute pancreatitis is a leading cause for hospital admissions in North America, with an annual incidence of 13 to 45 per 100 000 people(1). Patients diagnosed with moderate to severe acute pancreatitis have a mortality rate of 20-40%(1,2). Acute pancreatitis is an acute inflammation of the pancreas secondary to various many aetiologies, with the two most common aetiologies in North America being gallstone disease and alcohol use. Complications from acute pancreatitis can vary from local (peripancreatic fluid collections, pseudocysts, acute necrotic collections, walled-off necrosis, or infected necrotizing pancreatitis) to systemic (multi-system organ failure, and exacerbations of pre-existing comorbidities). These complications may result in prolonged hospital stays, intensive care admission and multiple invasive interventions such as endoscopic retrograde cholangiopancreatography (ERCP), image-guided percutaneous drainage, video-assisted retroperitoneal debridement (VARDs), endoscopic pancreatic necrosectomy, and open transgastric necrosectomy. As such, severe pancreatitis can result in a significant burden for the patient and the healthcare system.

Manitoba has two tertiary care centres located in Winnipeg—Health Sciences Centre (HSC) and St. Boniface Hospital. These sites accept patients from two provinces (Manitoba and Northern Ontario), and parts of the territory of Nunavut. Approximately 41% of Manitobans lived in a rural or small population centre in 2016(3). Many communities in Manitoba are remote and may only be accessible by air or water throughout the year. Northern Manitoba is defined as the region of Manitoba north of the 53rd parallel(4). Remote communities in Manitoba are defined as a community that is not connected to the provincial highway system by a year-round all-weather road(4,5). Given that a large proportion of our patient population are from rural, northern, and remote locations, it is important to examine whether patient outcomes are affected by rurality compared to their urban counterparts in terms of mortality, time to intervention, length of stay in hospital, and other complications. It is important to examine the factors associated with pancreatitis in Manitoba to identify potential patterns that can help improve care.

Previous literature has shown differences in outcomes for general surgical diseases between rural and urban patients. In a cross-sectional study conducted on patients admitted with choledocholithiasis, it was noted that rural patients were less likely to receive an intervention than urban patients (6). A study looking at acute appendicitis showed that regardless of socioeconomic status and country, rural patients had worse outcomes in terms of their disease severity(7). Conversely, a recent study in New Zealand looked at the effects of rurality and ethnicity on acute pancreatitis severity and outcomes and found no significant difference(8). The patient characteristics, healthcare system and

geographic location of New Zealand is different from Manitoba. For example, geographically Manitoba is 2.5 times the size of New Zealand, with 0.26 times the population. As the two referral sites are located close to one side of the province transportation times can be prolonged, often times extending to multiple days. Thus, access to care can be different and more challenging in Manitoba, which is why a study in Manitoba is needed. One population-based study done in Maryland, USA assessed the severity and mortality in patients with acute pancreatitis who were transferred versus not transferred to referral centres(9). They found that transferred patients had more severe pancreatitis with a higher overall mortality and that severity, race and age influenced a provider's decision to transfer a patient. With the limited and inconclusive data on rurality's affect on patient outcomes, this study will help contribute information towards the improvement of our health care systems to make surgical care more equitable in Manitoba.

Research Question and Objectives

Research question: Do patients with moderate to severe acute pancreatitis transferred from a rural, northern, or remote center to a tertiary care centre in Manitoba have different outcomes than an urban patient admitted with moderate to severe acute pancreatitis? Our null hypothesis was that there will be no significant difference between urban, rural, and northern/remote patients in terms of time to initial intervention.

Objectives:

- 1) Identify differences in times to initial intervention and its associated outcomes in patients with moderate-severe acute pancreatitis
- 2) Identify other risk factors that may contribute to worse outcomes (ex. geographic location or comorbidities)
- 3) Identify referral patterns from non-tertiary care centres for moderate-severe acute pancreatitis in Manitoba.

Primary Outcome: The time from initial presentation to a health care centre to initial intervention (percutaneous, surgical, or endoscopic performed at a tertiary care centre).

Secondary Outcome: 30-day mortality, time spent in referral hospital, time spent in tertiary care centre (date of admission to hospital until the date of discharge), combined time in hospital (referral + tertiary care centre), ICU admission, total number of interventions during the admission, types of interventions, cholecystectomy rates (during hospital stay or within 3 months from discharge), number of readmissions (up until 12 months post-initial discharge), transfer times to a tertiary care centre (if the patient came from a referral centre), demographics (age, sex, comorbidities), and urban or rural/northern/remote status (Manitoba Public Insurance has defined a list of remote communities, and any northern community is north of the 53rd parallel), and loss to follow-up by clinician.

Methodology

Study Design

This was a retrospective comparative cohort study with data retrieved from chart reviews within the last 3 years at HSC between July 1, 2017-June 30, 2020. The population assessed were patients admitted to a tertiary care centre in Winnipeg for acute pancreatitis. The inclusion criteria were patients 18 years or older with moderate-severe pancreatitis; must be admitted for ≥ 7 days or have died within 7 days and were admitted to the acute surgical care service. Patients diagnosed with chronic pancreatitis or were in hospital for < 7 days were excluded. The primary outcome being assessed was time from initial presentation to intervention (percutaneous, surgical, or endoscopic). Secondary outcomes included 30-day mortality, length of stay (LOS) in hospital, admission at a non-tertiary care centre prior to transfer to a tertiary centre, ICU admission, ICU LOS, total number of interventions, types of interventions done, cholecystectomy rates (index and interval), number of readmissions, transfer times to a tertiary care centre, and loss to follow-up by clinician within 1 year from discharge. Physical patient charts and electronic medical records were examined. In addition to the primary and secondary outcome measures, baseline demographic information was also recorded and input into the REDCap electronic data capture tool hosted at the University of Manitoba(10,11).

Pancreatitis severity (mild, moderate, and severe) was defined based on the Revised Atlanta classification (12). Readmission was defined as a patient being admitted within 1 year from initial discharge with a diagnosis pertaining to pancreatitis. Cholecystectomies were recorded as either done during the initial admission (index) or were done within 1 year from initial discharge (interval).

Data analysis

The statistical analysis was performed using SPSS version 28.0.1.1(13). Descriptive statistics was done for all variables. Categorical/nominal variables were described as proportions and underwent a univariate analysis using the Chi Square test. This included sex, comorbidities, acute pancreatitis severity, acute pancreatitis etiology, the proportion of interventions performed, types of interventions performed, number of readmissions, and number of cholecystectomies done. Continuous variables were presented as means and standard deviations and underwent analysis using a one-way ANOVA if parametric testing was appropriate or underwent a Kruskal-Wallis one way ANOVA for variables that were non-parametric (eg. time to first intervention, LOS, and transfer times). Significant results underwent a post-hoc analysis to determine where the significance was between groups. Variables found to be significant ($p < 0.05$) was then included in the multinomial logistic regression model.

Ethics Approval

Ethics Approval was obtained from the University of Manitoba Health Research Ethics Board (HREB) and the University of British Columbia Research Ethics Board (UBCREB). Applications were filed in January 2022 and the University of Manitoba HREB approval was obtained on January 27, 2022. The Ethics # is HS25322 (H2022:019). UBCREB was approved on March 29, 2022 and the ethics # is H22-00358. Given that the study was a retrospective chart review, no anticipated potential distress or hazards were anticipated that patients may potentially prospectively experience, thus, consent was not obtained prior to reviewing the charts. Data collected using REDCap was de-identified to ensure patient confidentiality using unique study identifiers. The master list linking the ID codes to the patients were stored on a password protected file on the University of Manitoba Sharepoint server. The master list will be stored for 7 years after the project is complete and then the data will be deleted. No direct patient identifying information was reported in the data analysis nor will it be in any published work.

Results

Patient characteristics

Between July 2017-June 2020, 62 patients were identified to be admitted with acute pancreatitis at HSC under the trauma and acute care surgery team with length of admissions equal or greater than 7 days. Using the patient's first 3 digits of their postal code, the patients were then categorized into urban, rural, or northern/remote groups. 32 (51.6%) were residing in an urban centre, 18 (29%) were in rural centres, and 12 (19.4%) lived in either northern or remote communities. Table 1

summarizes the basic patient demographics. There were equal proportion of males and females in the urban group, however, females made up approximately 72-75% of the rural and northern/remote group, showing a significant difference between the 3 groups ($p = 0.039$). There were no significant differences between groups in terms of age or comorbidities. Figure 1 is a graduated symbol map showing the distribution of the patients' geographic region of primary residence, with most of the distribution clustered around Winnipeg. As seen in the map, there were some patients who were transferred to HSC from out-of-province centres in Saskatchewan and northwestern Ontario either due to repatriation purposes or for ICU or surgical/endoscopic capabilities. Although HSC's catchment area includes Nunavut, no patients were admitted from Nunavut with acute pancreatitis during the study's time frame.

Table 1. Patient demographics and characteristics for patients admitted with acute pancreatitis to HSC between 2017-2020.

Patient characteristics	Urban	Rural	Northern/Remote	p-value
Number of patients, n (%)	32 (51.6)	18 (29.0)	12 (19.4)	
Sex				0.039*
Male, n (%)	16 (50.0)	5 (27.8)	3 (25.0)	
Female, n (%)	16 (50.0)	13 (72.2)	9 (75.0)	
Mean age (year) \pm SD	56.9 \pm 16.4	60.7 \pm 14.9	45.9 \pm 21.3	0.067
Comorbidities, n (%)				
Diabetes Mellitus	5 (15.6)	8 (44.4)	3 (25.0)	0.082
Hypertension	17 (53.1)	10 (55.6)	5 (41.7)	0.7347
Chronic renal disease	2 (6.3)	3 (16.7)	1 (8.3)	0.4817
Cardiovascular disease	9 (28.1)	7 (38.9)	3 (25.0)	0.6534
Dyslipidemia	7 (21.9)	7 (38.9)	3 (25.0)	0.4233
Chronic pulmonary disease	5 (15.6)	4 (22.2)	1 (8.3)	0.5948
Cerebrovascular accident	3 (9.4)	0 (0.0)	0 (0.0)	0.2281
GERD	13 (40.6)	3 (16.7)	5 (41.7)	0.1868
Other	10 (31.2)	10 (55.6)	6 (50.0)	0.2027

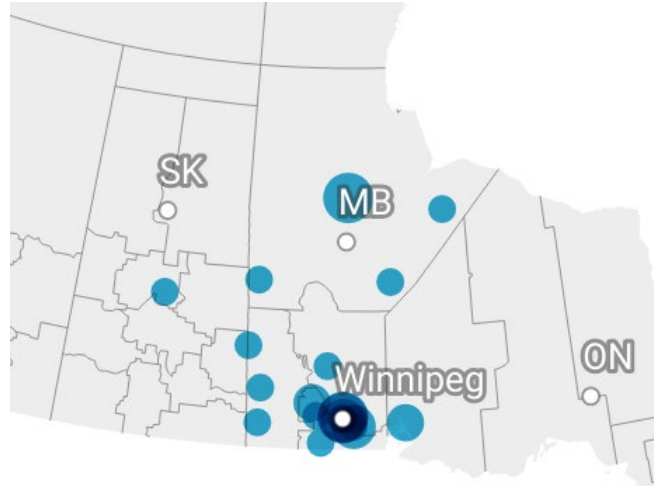


Figure 1. Graduated symbol map representing the patient's primary region of residence (created on DataWrapper)

Primary and Secondary Outcomes

Table 2 outlines the primary and secondary outcomes. There were no significant differences found between urban, rural, or northern/remote patients in terms of severity of their acute pancreatitis. Urban and rural patients mainly had gallstone pancreatitis, while the etiology of acute pancreatitis in northern/remote patients were more dispersed between gallstones, post-ERCP, and alcohol. However, no statistical significance was found between groups for the etiology of acute pancreatitis. Only 1 patient had acute pancreatitis secondary to trauma (rural group) and 3 patients did not have any documentation in the medical charts regarding the etiology of their acute pancreatitis. No significant difference was found in the proportion of patients who underwent an intervention (percutaneous, endoscopic, or surgical) during their admission. 71.9% of urban patients admitted underwent an intervention during their 1st admission, while 55.6% of rural and 50% of northern/remote patients underwent an intervention. Looking at our primary outcome, there was no significant difference in terms of time from initial presentation to intervention between urban, rural, or northern/remote patients. The types of interventions performed did not significantly differ either. A significant difference was found for transfer times to a tertiary care center ($p = 0.001$). A post-hoc analysis showed that the significant difference was between urban and rural patients (0.9 days versus 4.7 days, $p = 0.043$). Additionally, rural (44.4%) and northern/remote patients (50.0%) were found to be admitted to non-tertiary care centres prior to being transferred to a tertiary care centre significantly ($p = 0.012$) more frequently than urban patients (12.5%), however, no differences in length of stays at the non-tertiary care centres were found.

There was a significant difference between groups for ICU admissions ($p = 0.020$). A post-hoc analysis showed that rural patients had a significant difference XXX what difference? compared to urban

and northern/remote patients, but there was no significant difference between urban and northern/remote patients. There were no differences in the average ICU length of stay between groups. No significant differences were found for patients requiring readmissions or interventions performed during readmissions, nor in the 30-day mortality or loss to follow-up. The largest difference was found between urban and rural patients for cholecystectomies: Cholecystectomies were performed at a significantly higher rate amongst urban patients compared to rural and northern/remote patients ($p=0.016$). Although urban patients had a higher proportion of index cholecystectomies being done, no statistical difference was found between the 3 groups.

Table 2. Primary and secondary outcomes between urban, rural, northern/remote patients.

Outcomes	Urban	Rural	Northern/ Remote	P-value
Severity of acute pancreatitis, n (%)	32	18	12	0.284
Mild	12 (37.5)	3 (16.7)	5 (41.7)	
Moderate	16 (50)	9 (50.0)	4 (33.3)	
Severe	4 (12.5)	6 (33.3)	3 (25.0)	
Etiology of acute pancreatitis, n (%)				0.174
Gallstone	20 (62.5)	11 (61.1)	5 (41.7)	
Post-ERCP	5 (15.6)	2 (11.1)	4 (33.3)	
Alcohol	6 (18.8)	1 (5.6)	3 (25.0)	
Trauma	0 (0.0)	1 (5.6)	0 (0.0)	
Not documented	1 (3.1)	2 (11.1)	0 (0.0)	
Number of patients who underwent an intervention during 1st admission, n (%)	23 (71.9)	10 (55.6)	6 (50)	0.305
Time to first intervention, median (days)	6	8	4	0.897
Interventions performed in 1st admission, n (%)	26	12	9	0.305
Surgical debridement	7 (26.9)	4 (33.3)	1 (11.1)	
Endoscopic debridement	1 (3.9)	3 (25.0)	1 (11.1)	
Percutaneous drainage	0 (0.0)	1 (8.3)	2 (22.2)	
ERCP	5 (19.2))	2 (16.7)	2 (22.2)	
Laparoscopic cholecystectomy	13 (50.0)	2 (16.7)	3 (33.3)	
Mean transfer times to tertiary care centre (days) \pmSD	0.9 \pm 2.5	4.7 \pm 7.9	3.3 \pm 5.4	0.001*
Mean LOS (days) \pmSD	15.1 \pm 10.6	24.6 \pm 31.5	21 \pm 23.9	0.422
Admissions at other centre prior to transfer to tertiary care centre, n (%)	4 (12.5)	8 (44.4)	6 (50.0)	0.012*
Mean LOS (days) \pm SD	5.3 \pm 5.7	9 \pm 9.9	6.2 \pm 6.7	0.688
ICU admission, n (%)	3 (9.4)	7 (38.9)	1 (8.3)	0.020*
Mean ICU LOS (days) \pmSD	12 \pm 8.7	8.9 \pm 8.6	44	0.145

Number of patients readmitted within 1 year from initial discharge, n (%)	6 (18.8)	3 (16.7)	1 (8.3)	0.703
Mean number of readmissions amongst patients readmitted, n \pm SD	1.80 \pm 0.8	1 \pm 0.4	1 \pm 0.3	0.695
Mean number of interventions performed during readmission \pm SD	1.3 \pm 0.8	1 \pm 0.4	1 \pm 0.3	0.678
Cholecystectomy, n (%)	19 (59.4)	4 (22.2)	3 (25.0)	0.016*
Index (during 1st admission)	13 (40.6)	2 (11.1)	3 (25.0)	0.083
Interval (within 1 year from discharge)	5 (15.6)	2 (11.1)	0 (0.0)	0.246
Lost to follow-up in 1 year, n (%)	5 (15.6)	5 (27.8)	4 (33.3)	0.376
Mortality, n (%)	1 (3.1)	0 (0.0)	0 (0.0)	0.621

Discussion

The main goal of this study was to assess whether there were differences between urban, rural, or northern/remote patients admitted with acute pancreatitis to a tertiary care centre in Winnipeg, MB in terms of patient characteristics and outcomes. Given the large catchment area that HSC serves and how geographically spread out the communities are, it was reasonable to infer that there would be differences in presentation times and in patient outcomes as a result. A study assessing the effects of rurality and ethnicity in severity and outcomes in patients admitted with acute pancreatitis in New Zealand showed no significant differences in severity, length of stay, mortality, ICU admissions or etiology between urban and rural patients(8). Given the differences between New Zealand and Manitoba however, we expected there to be some differences in outcomes compared to that study.

There were no differences in severity, etiology, LOS, interventions performed, readmissions, and loss to follow-up between the three regional cohorts. No significant difference was seen in our primary outcome of time to intervention between urban, rural, or northern/remote patients. Significant differences in secondary outcomes were seen in the transfer times to a tertiary care centre, admissions to a non-tertiary care centre prior to transferring to a tertiary care centre, ICU admissions, and the rate of cholecystectomies. There was also a significant difference proportions of the sexes between groups.

Albeit, this study comprised of a small sample size, a few trends can be discussed. Our findings in terms of severity and etiology of acute pancreatitis was in keeping with previous studies(8). Finlayson *et al.* found that rural patients were willing to accept a higher risk of care at a local healthcare centre versus a lower risk at a regional/tertiary centre(14). This may explain why there was no significant difference in severity. Intuitively, we would have expected that patients admitted from rural or northern/remote areas would have presented in a delayed manner, resulting in greater severity. This

study would not have been able to capture the patient outcomes for a portion of the rural, northern/remote patients who opted to receive all their care in more local centres and were not transferred. Thus, another interesting study would be to assess whether severe acute pancreatitis patients are being treated at more local/rural care centres, and if so, what the outcomes are for those patients who are not transferred. We would examine the factors that we can optimize to improve the quality of care for patient locally.

Post-ERCP and alcohol were also found to be more common causes of acute pancreatitis amongst northern/remote patients. The risk of post-ERCP pancreatitis was found to be increased in patients who had a previous history of acute pancreatitis according to a systematic review done by Chen *et al*(15). Given the geographic isolation of northern/remote patients, those patients may potentially have experienced previous bouts of mild acute pancreatitis that did not result in immediate presentation to a healthcare facility but may have placed them at an increased risk for post-ERCP pancreatitis on subsequent presentations. Also of note, the Northern Regional Health Authority had the highest rate of substance use hospitalizations in Manitoba, which may lead to an increased proportion of patients from northern Manitoba having alcohol as an etiology of their acute pancreatitis. This data was not completely captured in this study, as patients admitted with acute pancreatitis secondary to alcohol would more likely be admitted to a medicine team instead of the surgical team.

As expected, the mean transfer times were significantly different with urban patients requiring <1 day to be admitted to a tertiary care centre compared to rural patients (4.7 days), and northern/remote patients (3.3 days). Rural patients are more likely to be transported on ground, whereas northern/remote patients are more likely to be transferred by air, which may explain the shorter transfer time for northern/remote patients. Not surprisingly, rural and northern/remote patients were more likely to be admitted to another hospital prior to being transferred to a tertiary care centre for further care. This was in keeping with previous studies showing that 80% of all hospitalizations in Manitoba were in the patient's region of residence(16). Although previous population data have shown that northern/remote patients have longer LOS in hospital(16), we did not appreciate any significant difference. Amongst all patients who were admitted to a non-tertiary care centre, no groups had a significantly different LOS before being transferred to a tertiary care centre, which implies that patients who required immediate transfer due to worsening pancreatitis symptoms did not experience significant delays secondary to their geographic location.

Rural patients were found to have a significantly higher proportion of ICU admissions compared to urban patients in the post-hoc analysis. As stated previously, patients tended to be hospitalized in

their region of residence but required transfer to a tertiary care centre should their disease severity need tertiary level care. In this study, rural patients were more likely to be admitted to a non-tertiary centre first, which means that patients who are transferred to HSC were likely sicker and had a higher risk of needing ICU level care. Although there was no significant difference in severity, rural patients did have the highest proportion of patients diagnosed with severe acute pancreatitis.

Interestingly, there was a significant difference in the total number of cholecystectomies performed between urban, rural, and northern/remote patients. The post-hoc analysis showed that urban patients had a significantly higher rate of cholecystectomies done, but there was no significant difference in the proportion of index versus interval cholecystectomies. Out of the 18 rural patients admitted, only 2 received a cholecystectomy in hospital, and 2 had it done after their discharge. Out of the 12 northern/remote patients admitted, all 3 patients who underwent a cholecystectomy had it done during their admission. No northern/remote patients had an interval cholecystectomy. Patients from rural, northern/remote patients may have more severe presentations that preclude them from having an index cholecystectomy during their initial admission. Additionally, the patient's region of residence may affect their ability to have an interval cholecystectomy due to various barriers associated with geographic remoteness. There may be less surgeon availability in rural or non-tertiary care centres that can provide an interval cholecystectomy.

A strength of this study is that data is being extracted from one of only two tertiary care centres, so nearly all severe pancreatitis patients are admitted at these two sites. Additionally, all ERCPs are only done at these two tertiary care sites. Universal health care is also present, making the outcomes not affected by the patient's payor status, especially for the consideration of an interval cholecystectomy. Overall, further studies should assess the factors and barriers that may affect rural, northern, and remote patients in receiving an index or an interval cholecystectomy, since a cholecystectomy could significantly reduce their risk of future gallstone complications.

Limitations

This study had various limitations. This study was intended to examine all acute pancreatitis patients admitted to both tertiary care centres in Manitoba (HSC and St. Boniface Hospital) in both surgical and medical wards over the span of 5 years between 2015 to 2020. Only patients admitted to a surgical team at HSC between 2017 to 2020 were reviewed for this project. Additional patients at the second tertiary hospital and patients admitted to a medical team were not included. The small patient

population limits the power of the study to identify statistical differences (ie. ICU LOS). More charts will be reviewed in the future to include all the intended patients to increase the sample size. Furthermore, this was a retrospective study, which has an increased risk for missing data, recall bias, other confounders that were not measured in the chart review, and the inability to assess the temporal relationship in a patient's admission.

Recommendations

Further study is needed to obtain a larger population size for this study. Additionally, future studies assessing transfer times for rural patients to a tertiary care centre in Winnipeg is needed in addition to assessing factors that may influence the increased proportion of ICU admissions amongst rural patients compared to northern/remote and urban patients. Variables and barriers that result in a lower cholecystectomy rate in rural and northern/remote patients should also be explored to ensure equitable surgical care throughout Manitoba. Larger prospective studies would be useful to confirm this study's findings. Population level data would have also been interesting to analyze to determine whether there were confounders that could not have been captured in a retrospective review.

Conclusion

Acute pancreatitis can present in a multitude of ways, resulting in some patients requiring more invasive and intensive care that can only be provided at a tertiary care centre. This study showed no difference in our primary outcome in terms of the time from initial presentation to initial intervention. However, rural, northern, and remote patients were more likely to be admitted to another centre prior to admission to a tertiary care centre and are at a higher risk for ICU admissions. Urban patients, however, are more likely to have a cholecystectomy performed for their acute pancreatitis compared to rural, northern, and remote patients in Manitoba. Overall, this study attempted to assess variables that may influence an acute pancreatitis patients' outcome and in turn, identify areas that need further study to ensure patients are receiving equitable care no matter where their region of residence is.

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