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Early Outcome of Treatment of Chronic Mesenteric Ischemia

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There are limited data regarding long-term outcomes of chronic mesenteric ischemia (CMI) of the intestine. We sought to identify treatment outcomes of CMI. The NIS database was used to identify patients admitted for the diagnosis of CMI between 2002 and 2012. Multivariate analysis using logistic regression was performed to quantify outcomes of CMI. A total of 160,889 patients were admitted for chronic vascular insufficiency of intestine; of which 7,906 patients underwent surgical/endovascular treatment for CMI. Among patients who underwent surgery 62 per cent had endovascular treatment and 38 per cent had open vascular treatment. Need of open surgery (adjusted odds ratio (AOR): 5.13, P < 0.01) and age ‡70 years (AOR: 3.41, P < 0.01) had strong associations with mortality of patients. Open vascular treatment has higher mortality (AOR: 5.07, P < 0.01) and morbidity (AOR: 2.14, P < 0.01). However, endovascular treatment had higher risk of postoperative wound hematoma (AOR: 2.81, P < 0.01). Most patients admitted for CMI are treated with endovascular treatment. Endovascular treatment has the advantage of lower mortality and morbidity. Need to open surgery and age ‡70 years have strong associations with mortality of patients.

CHRONIC MESENTERIC ISCHEMIA (CMI) is an uncommon condition that accounts for approximately 5 per cent of all mesenteric ischemia events.^{1,2} Patients usually present with nonspecific symptoms, often with a significant delay in diagnosis.³ The clinical consequences of not recognizing the disease and delay in treating patients include weight loss, malnutrition, and bowel necrosis.^{1,2} It is important to diagnose patients early to decrease the associated morbidity and mortality. Identification of risk factors for CMI with the goal of identifying patients during earlier stages of their disease was the focus of a large number of studies.^{2,4} However, there is limited information regarding longterm outcomes of such patients.

Among treatment options for CMI, definitive therapy is usually preferred to minimize consequences of the disease. Among definitive treatment options, endovascular therapy has rapidly expanded during the last decade. However, the controversy regarding the type of revascularization (open versus endovascular) and effects of medical management in patients' treatment persists. ^{2, 4–8} A number of studies have attempted to compare endovascular therapy with open operation, but are also are limited by the small sizes of the study population; and a nationwide study comparing treatment methods of CMI is lacking. ^{8–13} Therefore, we aim to report early outcomes of treatment of CMI and compare the methods of treatment.

Patient Population and Methods

This study was performed using the Nationwide Inpatient Sample (NIS) database14 from January 1, 2002 to December 31, 2012. The health care cost and utilization project of NIS is an inpatient care database in the United States with approximately 20 per cent stratified samples of American community, nonmilitary, and nonfederal hospitals, resulting in a sampling frame that approximates 95 per cent of all hospital discharges in the United States. ¹⁴ We looked at adult patients (age \$18 years) who were admitted with diagnosis of chronic vascular insufficiency of the intestine using the diagnosis code of 557.1 as specified by the ICD-9 clinical modifications (ICD-9-CM) and underwent elective surgical treatment of CMI. Procedures were defined based on the following ICD-9 procedure codes: open vascular procedures (3816, 38.36, 38.46, and 39.26), endovascular procedures (39.50, 39.90). Patients who had concomitant acute and CMI, were younger than 18, and patients underwent aortic reconstruction (38.14, 39.54, 38.84, 38.84, 3834, and 3844) were excluded from the study (Fig. 1).

Preoperative factors analyzed included patient characteristics (age, sex, and race), patient comorbidities [history of congestive heart failure (CHF), chronic renal failure (CRF), diabetes mellitus with or without complications, weight loss more than 10 per cent in last six months, history of severe pulmonary disease, coagulopathy (coexisting coagulopathy conditions that are not directly related to the principal diagnosis, or the main reason for admission, and are likely to have originated before the hospital stay), history of peripheral vascular disorders, fluid and electrolyte disorders, hypertension (HTN), liver disease, history of coronary artery disease, hypothyroidism, cardiac valvular disease, anemia deficiency, and chronic blood loss anemia]. Surgical procedures included balloon angioplasty, endovascular stenting, endarterectomy, vascular bypass, resection of vessel with direct anastomosis, resection of vessel with replacement. Postprocedural complications included pneumonia, myocardial infarction, prolonged ileus, urinary tract infection, disseminated intravascular coagulation (DIC), bowel infarction need to resection, respiratory failure, need for packed cell transfusion, wound hematoma (incisional site hematoma with or without need for transfusion), hemorrhage (intraoperative or postoperative hemorrhagic complications with or without need for transfusion that complicated the procedure), upper gastrointestinal bleeding (GIB) (bleeding with the sources of esophagus, gastric, and duodenum), lower GIB (after ligament of Treitz), and acute renal failure (ARF). The demographic data and the most common comorbidities of patients were identified. The hospital charges, hospital length of stay, post procedural complications, and in hospital mortality of patients by procedure type were examined. Risk adjusted analysis was performed to identify independent predictors of mortality after CMI. Male gender, and age <70 years were used as reference data points for comparison in line with the literature. 15, 16

Statistical Analysis

Statistical analysis was performed with SPSS® software, Version 22 (SPSS Inc., Chicago, IL). Logistic regression analysis was used to estimate the association between type of the procedures and each outcome, including in-hospital mortality and all of the

considered postoperative complications. P values less than 0.05 were considered statistically significant. For each outcome, the adjusted odds ratio (AOR) with a 95 per cent confidence interval (CI) was calculated and reported to estimate the relative risk. Adjustments were made for history of peripheral vascular disorders, diabetes mellitus, chronic lung disease, coronary artery disease, weight loss, hypothyroidism, cardiac valvular disease, anemia deficiency, chronic blood loss anemia, CHF, CRF, HTN, fluid and electrolyte disorders, liver disease, coagulopathy, need for packed cell transfusion, treatment technique (endovascular versus open surgery), age, sex, and race.

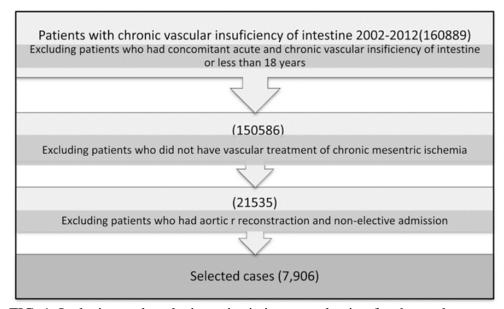


FIG. 1. Inclusion and exclusion criteria in case selection for the study.

Results

A total of 160,889 patients were admitted for chronic vascular insufficiency of intestine between 2002 and 2012, of which 7,906 patients who underwent elective surgical treatment of CMI were sampled. Over the 11-year study period, the number of patients surgically managed increased from 437 in 2002 to 925 in 2012. The median age of the patients was 70 years, and 52.9 per cent of the patients were \$70 years of age; the majority of the patients were Caucasian (86.4%) and female (73.4%). The most common comorbidities include peripheral vascular disorders (67.4%), HTN (66.4%), and coronary artery disease (39.5%). The demographic data of patients were reported in Table 1.

Endovascular treatment in 62 per cent of the study population was the most common treatment of patients admitted with diagnosis of CMI. Also, percutaneous balloon angioplasty and stenting was used in 73.6 per cent of the endovascular treatments. Over the 11-year study period, there was a steady increase in CMI patients undergoing endovascular treatment from 223 in 2002 to 635 in 2012 (Fig. 2).

Over the 11-year study period, the most common open surgical procedure was vascular bypass (91.5%) followed by endarterectomy (13.2%). The percentage of CMI patients underwent bowel resection was 0.8, and there was no significant decrease in rate of bowel resection over the 11-year study period (2% in 2002 vs 1.6% in 2012).

A total of 105 patients (1.3%) underwent both endovascular and open treatment of CMI. There was a steady decrease in the percentage of CMI patients who underwent both treatment methods from 3.42 in 2002 to 0.92 in 2012.

The median length of stay in the hospital was four days. For patients undergoing endovascular treatment, the median length of stay in the hospital was two days, whereas for patients with open vascular procedures it was eight days. The adjusted mean difference in hospitalization was six days higher (CI: 5.86-6.60, P < 0.01).

The overall mortality rate in patients with CMI was 2.9 per cent. The mortality rate in patients with open vascular treatment and endovascular treatment was 5.5 per cent and 1.1 per cent, respectively. The adjusted risk of mortality in patients with open vascular treatment was estimated to be more than five times that of endovascular treatment (AOR: 5.13, P < 0.01). When compared with patients without bowel resection, patients who had bowel resection had a significantly higher mortality rate (AOR: 3.57, P < 0.01).

Table 1. Demographics of Patients Who Were Electively Admitted with CMI and Underwent Surgical Treatment in the United States, NIS 2002 to 2012

	Patients Characteristics	Endovascular Treatment (4,903)	Open Vascular Procedures (3,108)	P Value
Age	Mean, year	72 ± 11	65 ± 13	_
	Median, year	72	67	_
	Age >70 year (%)	2967 (60.5)	1254 (40.3)	< 0.01
Sex	Female (%)	3529 (72)	2348 (75.6)	< 0.01
Race	White (%)	3315 (67.6)	2140 (68.8)	0.08
	Black (%)	165 (3.4)	117 (3.8)	0.20
	Hispanic (%)	167 (3.4)	94 (3)	0.41
	Asian or Pacific Islander (%)	54 (1.1)	21 (0.7)	0.04
	Other (%)	115 (2.4)	73 (2.4)	0.87
Comorbidity	Peripheral vascular disorders (%)	3573 (72.9)	1832 (58.9)	< 0.01
•	HTN (%)	3379 (68.9)	1931 (62.1)	< 0.01
	Coronary artery disease (%)	2234 (45.6)	930 (29.9)	< 0.01
	Chronic pulmonary disease (%)	1304 (26.6)	997 (32.1)	< 0.01
	Diabetes (%)	1107 (22.6)	525 (16.9)	< 0.01
	Fluid and electrolyte disorders (%)	665 (13.6)	906 (29.2)	< 0.01
	CRF	654 (13.3)	256 (8.2)	< 0.01
	Weight loss (%)	482 (9.8)	698 (22.5)	< 0.01
	Deficiency anemia (%)	570 (11.6)	455 (14.6)	< 0.01
	Hypothyroidism (%)	516 (10.5)	265 (8.5)	< 0.01
	Coagulopathy (%)	95 (1.9)	376 (12.1)	< 0.01
	CHF	484 (9.9)	277 (8.9)	0.28
	Cardiac valvular disease (%)	321 (6.5)	108 (3.5)	< 0.01
	Chronic blood loss anemia (%)	59 (1.2)	47 (1.5)	0.12
	Liver disease (%)	41 (0.8)	53 (1.7)	< 0.01
Procedure	Angioplasty (%)	4903 (100)		_
	Angioplasty with stent (%)	3610 (73.6)	_	_
	Vascular bypass (%)		2845 (91.5)	_
	Small bowel resection	_	51 (1.7)	_
	Endarterectomy (%)	_	410 (13.2)	_
	Resection of vessel with replacement (%)	_	19 (0.6)	_
	Resection of vessel with anastomosis (%)	_	11 (0.4)	_

Also, over the 11-year study period there was a steady decrease in the mortality rate of patients. Mortality rate of open vascular treatment of CMI decrease from 12.22 per cent in 2002 to 5 per cent in 2012. Mortality rates of surgical treatments of CMI during 2002 to 2012 are displayed in Fig. 3.

Patients who had open vascular procedures had higher mean total hospital charge compared with patients with endovascular treatment (\$103,338 vs \$55,605). The adjusted mean difference in hospital charge was \$31,121 higher (CI: 26835-35407, P < 0.01).

The risk-adjusted analysis for factors associated with higher mortality rates in patient with CMI is reported in Table 2. DIC (AOR: 14.87, P < 0.01), the need for open vascular surgery (AOR: 5.13, P < 0.01), and age \$70 years (AOR: 3.41, P < 0.01) were the strongest mortality predictor. Comorbidities having strong correlation with mortality of patients include CHF (AOR: 3.64, P < 0.01), coagulopathy (AOR: 2.55, P < 0.01), and fluid and electrolyte disorders (AOR:

2.52, P < 0.01).

The risk-adjusted analysis for postoperative complications in patient with CMI is reported in Table 3. In comparison of post procedural complications between endovascular group and open vascular procedures group, prolonged ileus (AOR: 7.16, P < 0.01), deep vein thrombosis (DVT) (AOR: 5.85, P < 0.01), and need for transfusion (AOR: 5.47, P < 0.01), were higher in the open vascular procedure group. However, postoperative lower GBI was significantly higher after endovascular treatment (AOR: 6.95, CI: 3.91-12.34, P < 0.01).

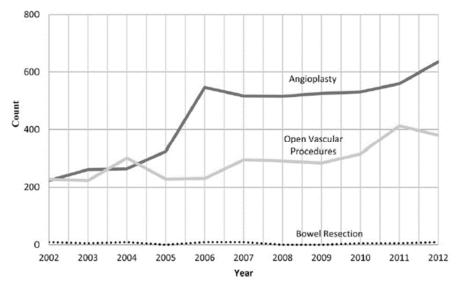


FIG. 2. Procedure volume for CMI during 2002 to 2012.

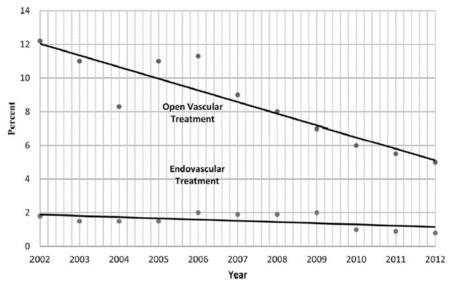


FIG. 3. Mortality rates of surgical treatments of the CMI during 2002 to 2012.

Table 2. Risk-Adjusted Analysis for Mortality Predictors of Patients with CMI Who Underwent Surgical Treatment

Patient-Specific Factors		AOR	95% CI	P Value
Gender	Female	Reference	Reference	Reference
	Male	1.45	1.05-2	0.02
Age	≤70	Reference	Reference	Reference
_	≥70	3.41	2.48-4.68	< 0.01
Comorbidity	No comorbidities	Reference	Reference	Reference
	Coagulopathy	2.55	1.72 - 3.77	< 0.01
	Fluid and electrolyte disorders	2.52	1.85 - 3.44	< 0.01
	CHF	3.64	2.49-5.32	< 0.01
	Hypothyroidism	2.31	1.50-3.56	< 0.01
	Coronary artery disease	1.39	1.02 - 1.88	0.03
	Peripheral vascular disorder	1.60	1.17 - 2.20	< 0.01
	Chronic blood loss anemia	1.92	0.76 - 4.85	0.16
	Renal failure	0.76	0.47 - 1.24	0.27
	Weight loss	1.02	0.72 - 1.45	0.88
	Liver disease	1.21	0.39 - 3.70	0.73
	Diabetes	1.22	0.85 - 1.74	0.26
	Chronic lung disease	0.69	0.50 - 1.02	0.05
	Deficiency anemia	0.79	0.53 - 1.17	0.25
	Cardiac valvular disease	0.40	0.19 - 1.02	0.05
	HTN	0.41	0.30 - 1.05	0.05
Repair technique	Endovascular	Reference	Reference	Reference
•	Open	5.13	3.61-7.28	< 0.01
Packed cell transfusion	No	Reference	Reference	Reference
	Yes	1.17	0.85 - 1.61	0.31
Other factors	DIC	14.87	5.58-39.66	< 0.01

Table 3. Risk-Adjusted Analysis of Outcomes of Open Vascular Treatment of CMI Compared with the Endovascular Treatment

Complication	Endovascular Treatment (4903)	Open Vascular Treatment (3108)	AOR	95% CI	P Value
In hospital mortality (%)	54 (1.1)	172 (5.5)	5.07	3.57-7.21	< 0.01
Overall morbidity (%)‡	908 (18.5)	1221 (39.2)	2.14	1.89 - 2.42	< 0.01
Bowel infarction need to resection (%)	13 (0.3)	51 (1.7)	4.63	2.35 - 9.10	< 0.01
Hospitalization >30 days (%)	45 (0.9)	168 (5.4)	3.53	2.33 - 5.36	< 0.01
Pneumonia (%)	72 (1.5)	205 (6.6)	2.82	2.03 - 3.91	< 0.01
Prolonged ileus (%)	104 (2.1)	465(14.9)	7.16	5.58-9.18	< 0.01
Hemorrhage (%)*	79 (1.6)	113 (3.7)	1.45	1.01-2.15	0.04
Wound hematoma (%)†	257 (5.2)	70 (2.3)	0.31	0.23 - 0.43	< 0.01
Respiratory failure (%)	82 (1.7)	217 (7)	2.67	1.97 - 3.63	< 0.01
ARF (%)	220 (4.5)	277 (8.9)	1.79	1.42 - 2.24	< 0.01
Urinary tract infection (%)	146 (3)	225 (7.2)	1.68	1.30-2.16	< 0.01
Upper GIB (%)	11 (0.2)	11 (0.3)	1.39	0.36 - 5.40	0.63
Lower GIB (%)	87 (1.8)	19 (0.6)	0.12	0.06 - 0.22	< 0.01
DIC (%)	11 (0.2)	18 (0.5)	1.99	0.01 - 4.70	0.83
DVT (%)	11 (0.2)	25 (0.8)	5.85	2.60-13.16	< 0.01
Myocardial infarction (%)	93 (1.9)	71 (2.3)	0.77	0.52 - 1.13	0.19
Need for transfusion (%)	442 (9)	1037 (33.4)	5.47	4.74-6.30	< 0.01

^{*} Intraoperative or postoperative hemorrhagic complications with or without need for transfusion that complicated the procedure.

Discussion

There was also a steady increase in the number of CMI patients undergoing surgical treatments. The number of the patients surgically treated in 2012 was twice that of 2002. Our study further shows an increase in the number of patients with a diagnosis of vascular insufficiency of intestine during 2002 to 2012. This is in line with the gradually increased number of patients diagnosed with CMI reported between 1988 and 2006.15 Also, surprisingly more than 70 per cent of patients underwent surgical treatment of CMI

y Incisional site hematoma with or without need for transfusion.

z Include hospitalization >30 days, pneumonia, prolonged ileus, postoperative hemorrhage, postoperative wound hematoma, respiratory failure, ARF, urinary tract infection, upper and lower GIB, DVT, and myocardial infarction.

are female. Further studies are indicated to investigate the reason of higher rate of CMI in females.

Endovascular treatment has evolved to be the most common interventional treatment of CMI. Over the 11-year study period, there was a steady increase in the number of CMI patients undergoing endovascular procedures (Fig. 1). This trend is consistent with the reported steadily increased rate of endovascular procedures and decreasing open procedures during 1988 to 2006 in the USA.¹⁵

There are associations between CMI and peripheral vascular disorders, HTN, and ischemic heart disease. Our study results show 67.4 per cent of patients with CMI have peripheral vascular disorders and 45.8 per cent of patients with CMI have both HTN and peripheral vascular disorders. In patients with chronic abdominal pain who had comorbidities of peripheral vascular disorders, HTN, or ischemic heart disease the diagnosis of CMI should be rolled out.

Our study results show the overall mortality rate in patients with CMI was 2.9 per cent. This is in line with the report of mortality rate of 2.6 per cent by Tallarita.8 Tallarita in a study of 187 patients who underwent surgical treatment of CMI reported mortality rate of 2.6 per cent. Also, we found a decrease in mortality rate of patients underwent surgical treatments of CMI especially open vascular treatment during 2002 to 2012 (Fig. 3). Overall mortality rate of treatment of CMI decreases from 7.3 per cent in 2002 to 2.2 percent in 2012. Surprisingly, the decrease in mortality rate was higher in open vascular treatment compared with endovascular treatment (Fig. 3). It can be explained by improved perioperative care over the 11-year study period.

Using the power of the large NIS database, this study identified significant predictors of mortality of CMI. The strongest predictor of mortality is need for open vascular technique and age \$70 years. This study also confirms the previous report of CHF, and age as the risk factors of mortality of patients by Schermerhorn and Tallarita^{8, 15} and adds coagulopathy, DIC, coronary artery disease, fluid and electrolyte disorders, hypothyroidism, and peripheral vascular disorder to the mortality predictors. Some mortality predictors such as hypothyroidism and fluid and electrolyte disorders are reducible and controlling such factors may decrease mortality of CMI patients who underwent surgical treatment.

Among comorbidities CHF was the most important mortality predictor of treatment of CMI. CHF has been introduced as a mortality predictor of treatment of CMI previously by Schermerhorn. In terms of coagulation abnormalities we found significantly higher mortality risks in patients who had preoperative coagulopathy as well as postoperative DIC. This reinforces the important effect of coagulation factors in outcomes of vascular procedures. Also, in comparison of open treatment of CMI with endovascular treatment, we found a two times higher rate of DIC after open treatment. However, after multivariate analysis we did not find any associations between open treatment and postoperative DIC. Further studies are indicated to see whether intensive correction of the coagulation abnormalities can decrease mortality of patients.

Preventive methods for postoperative renal failure should be considered for patients who are candidates of surgical treatment of CMI. The most common postoperative complication of endovascular treatment of CMI and the second most common complication in open treatment was ARF. This is in line with a previous

report regarding renal failure as a common complication of treatment of CMI.¹⁵ Although incidence of ARF in endovascular treatment is much lower than for open vascular procedures, 4.5 per cent of patient in the endovascular group still developed ARF.

The differences between the indications of open vascular surgery and endovascular treatment make the comparison of these treatment methods difficult; however, endovascular treatments seem to be a preferred choice compared with open vascular procedures when both treatment options are possible. In our study, even though the endovascular group was older and had more comorbidities (HTN, diabetes, peripheral vascular disorders, CRF, coronary artery disease, and CHF), their morbidity and mortality were significantly lower than the open group (Table 1). Also, open vascular procedures are associated with higher in-hospital charges, postoperative pneumonia, respiratory failure, DVT, prolonged ileus, and ARF. Lower mortality and morbidity rates for endovascular treatment compared with open surgery have been reported by previous studies. ^{2, 12, 15, 17–20} However, differences in disease stage between patients undergoing endovascular and open vascular treatment can overestimate mortality and morbidity of patients underwent open vascular repair.

We observed a decrease in the number of patients who underwent both open and endovascular treatment of CMI during the same hospitalization over the 11-year study period. It may be related to the advances in endovascular treatment over time.

Overall, bleeding complications were higher in open treatment of CMI compared with endovascular treatment. Higher rates of bleeding complications for open treatment compared with endovascular treatment have been reported by Schermerhorn previously. 15 However, the rate of incisional or puncture cite hematoma was significantly higher in endovascular treatment compared with open treatment. Puncture site hematoma has been reported as the most common complication of endovascular treatment of CMI multiple times. ^{21–23} In terms of GIB complication, when comparing open and endovascular treatments regarding upper GIB complication there was not any significant difference between the two types of treatment. However, our results show postoperative lower GIB was significantly higher in endovascular treatment of CMI compared with open vascular surgery. Lower GIB after endovascular treatment of CMI has been reported previously. It was explained with reperfusion hemorrhage after endovascular treatment. 21 Moore 21 in explanation, reported chronic ischemia may lead to changes in distal branch vessels which, complicated by failure of normal autoregulation, are susceptible to bleeding when suddenly exposed to the increased blood flow and pressures associated with restoration of circulation. Further studies are indicated to investigate the mechanisms of lower GIB after treatment of CMI and explain the higher rate of lower GIB in endovascular treatment compared with open treatment.

Finally, this study reinforces the importance of controlling reducible mortality predictors of hypothyroidism, coagulopathy, and fluid and electrolyte disorders before surgical treatment of CMI and endovascular treatment should be evaluated as the first choice of surgical treatment in possible situations.

Study Limitations

This study is a retrospective review and is therefore subject to typical biases for retrospective studies. The NIS is a database that collects information from over a

thousand hospitals and surgeons in the United States, and there is a wide variety in hospital settings and surgeons' expertise, and obvious selection bias in treatment choice for a given patient that can affect the study. Also, we lack outpatient follow-up data and long-term outcomes. Patients with CMI were defined using the diagnosis code of 557.1 as specified by (ICD-9-CM). However, there is an overlap between coding of CMI and ischemic colitis. Because of the overlap, we could not identify the group of patients who only had nonoperative treatment of CMI. However, by using the ICD-9 procedure codes specified for surgical treatment of CMI, which are not used in treatment of ischemic colitis, we could effectively exclude ischemic colitis patients from the study. This study compared complications of open vascular treatment of CMI with endovascular treatment. However, differences in indications, patient's populations, and disease stage in these two treatment groups make comparison of these treatment methods difficult. Also, coding errors may exist because of the use of discharge data. Despite these limitations; this study is one of the first to report on CMI specifically in this population subset.

Conclusion

Over the 11-year study period, there was a steady increase in the number of CMI patients who underwent surgical treatment for CMI, especially endovascular procedures. This study identified significant predictors of mortality of CMI. Need for open vascular repair in elderly is a poor prognostic situation with high mortality rate. Endovascular treatment is the most common procedure for treatment of CMI. We observed a decrease in the number of patients who underwent both open and endovascular treatment of CMI during the same hospitalization over the 11-year study period. Although differences of indications in open vascular surgery and endovascular treatment make comparison of these treatment methods difficult, patients who underwent endovascular treatment have lower mortality and morbidity rates. However, endovascular treatment has a significant higher rate of postoperative lower GIB and incisional cite hematoma compared with the open vascular treatment. In terms of open vascular treatment, there was a significant decrease in the mortality rate of patients who underwent open vascular treatment during 2002 to 2012, which may be related to improved perioperative care. Finally, our results show 67.4 per cent of patients with CMI have peripheral vascular disorders, an observation that may help with diagnosis of CMI in patients suffering from chronic abdominal pain.

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