An assessment of endoscopic and concomitant management of acute variceal bleeding at a tertiary care centre

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BACKGROUND: Several therapies have been demonstrated to be beneficial in the management of acute variceal bleeding (AVB). The aim of the present study was to characterize the use of these therapies at a Canadian tertiary care centre.

PATIENTS AND METHODS: A comprehensive chart review was performed to assess the management of all adult cirrhotic patients with AVB who were admitted to a university-affiliated, tertiary care centre between April 2001 and March 2004.

RESULTS: A total of 81 AVB patients were identified with a mean age of 53.7±13.2 years and a median model for end-stage liver disease score of 14. Endoscopy was performed within 8.2±7.6 h of admission. Vascular banding was performed for 87% of patients with esophageal varices, which were the most common source of bleeding (80%). Octreotide was used in 82% of patients for a mean duration of 74.3±35.4 h; prophylactic antibiotics were used in 25% of patients and beta-blockers were used in 24% of patients without any contraindications. Follow-up endoscopy was arranged for 46 of 71 (65%) survivors. Prophylactic antibiotic use was associated with the presence of ascites, while beta-blockers were used more often in the last year of the study.

CONCLUSIONS: There is a disconnection between the use of evidence-based recommendations and routine clinical practices in the management of AVB. Deficiencies identified include the lack of use of prophylactic antibiotics and beta-blockers, variable use of octreotide and inadequate follow-up recommendations. There is a need to identify measures to improve the process of care for patients with AVB which would ensure optimal management of these patients.

Key Words: Antibiotic prophylaxis; Beta-blockers; Clinical practice; Secondary prophylaxis; Variceal bleeding

A cute variceal bleeding (AVB) is one of the most serious and life-threatening complications of cirrhosis. Traditionally, the mortality rate associated with each episode of AVB was reported as being approximately 30% to 60% but several studies (1-7) have shown that the mortality rate secondary to variceal hemorrhage has dropped to approximately 15% to 20%. The improvement in outcomes after an episode of AVB is likely related to several recent additions to the therapeutic armamentarium which include resuscitative, endoscopic, adjunctive pharmacological and radiological therapies (3,4,6). Early endoscopic hemostasis accompanied by concomitant use of vasoactive agents and prophylactic antibiotics, followed by endoscopic eradication of varices and use of nonselective beta-blockers, have been individually shown to improve the outcomes for patients with AVB. There are also several practice guidelines that outline the appropriate care for persons presenting with AVB, which consist of prompt endoscopic hemostasis, concomitant use of vasoactive agents and antimicrobial prophylaxis, and subsequent endoscopic eradication of esophageal varices along with the use of nonselective beta-blockers (8-13). However, there are limited data to characterize the adherence of clinicians to these recommendations and advances in the management of AVB.
Therefore, we sought to analyze the process of care for patients presenting with AVB at a Canadian tertiary care centre and identify whether currently accepted standards of care were being met.

PATIENTS AND METHODS
A retrospective chart review was performed to identify all adult patients admitted to a university-affiliated, tertiary care centre between April 2001 and March 2004 with the primary diagnosis consistent with AVB. The study was conducted at the Winnipeg Health Sciences Centre, which is a tertiary care, university-affiliated hospital located in Winnipeg, Manitoba, that serves a catchment population of approximately 1.5 million persons.

Search strategy
All charts for persons admitted with a primary diagnosis of cirrhosis, chronic or alcoholic liver disease, gastrointestinal hemorrhage, esophageal varices or varices of other sites as identified by the International Classification of Diseases – Ninth Revision (ICD-9) codes (Table 1) were reviewed. After reviewing the charts of all cirrhotic patients hospitalized between April 2001 and March 2002, it was discovered that episodes of variceal bleeding could be identified with high sensitivity by limiting the search strategy to the ICD-9 codes for esophageal varices and ‘varices of other sites’ (ICD-9 codes 456.0, 456.1, 456.2x and 456.8). Therefore, it was decided to limit the chart review for subsequent years, that is, after March 2002, to these specific ICD-9 codes.

Data abstraction
Data were abstracted on patient demographics, marital status, current living situation, ongoing alcohol use, etiology of cirrhosis and results of pertinent laboratory studies on admission. Information was also collected on the endoscopy performed, specifically, the time between initial presentation and performance of endoscopy, the endoscopic diagnosis and the type of therapeutic modality used, if any. The use of intravenous octreotide, prophylactic antibiotics and beta blockade was tracked, as well as the physician’s recommendations regarding medical care following discharge. If a single patient had multiple hospital admissions for the treatment of AVB, data were extracted only on the initial episode.

Data analysis
The utilization of various endoscopic therapies, including endoscopic variceal ligation (EVL), sclerotherapy or injection of cyanoacrylate glue, was determined. The lag time between the time of initial presentation to hospital and performance of endoscopy was calculated, as was the proportion of patients who received endoscopic assessment within 24 h of presentation. The prevalence of various pharmacological interventions, including the use of octreotide, prophylactic antibiotics and nonselective beta-blockers in patients without a known contraindication to beta blockade, including reactive airway disease or known bradyarrhythmia, was determined.

The severity of underlying liver disease was determined by calculating each patient’s model for end-stage liver disease (MELD) score. The outcomes were determined in terms of duration of hospitalization, in-hospital mortality, as well as the rates of rebleeding and mortality within six months of the index episode of variceal bleeding.

NCSS 2004 (Number Cruncher Statistical Systems, USA) was used for statistical analysis. Means and SDs were calculated for normally distributed continuous data. **t** test and the Mann-Whitney **U** test were used to assess for statistical significance when categorical variables were compared, while Student’s **t** test and the Mann-Whitney **U** test were used to assess the significance of comparisons made between normally and non-normally distributed continuous data, respectively. Univariate and stepwise multivariate logistic regression analysis was performed to determine the predictive factors for the use of prophylactic antibiotics, octreotide infusion and secondary prophylactic beta blockade.

RESULTS
There were 81 patients who were admitted with AVB between April 2001 and March 2004, 65 (80%) of whom bled from esophageal varices, nine (11%) from gastric varices, four (5%) from both esophageal and gastric varices, and three (4%) from ectopic varices (Figure 1). Twenty-eight per cent of patients with AVB were admitted to a monitored bed. Demographic data for AVB patients did not differ from cirrhotic patients admitted for other indications (Table 2). Other common indications for

![Figure 1) Sites of bleeding varices](image-url)
admission of patients with cirrhosis (with or without AVB) are provided in Table 3.

Patient information concerning their social support and social habits were available for 76 (94%) patients, 32% of whom lived alone and 56% of whom had ongoing alcohol use at the time of presentation.

Endoscopy for AVB

The mean time from initial presentation to hospital until performance of endoscopy was 8.2±7.6 h. Fifty-eight percent of patients had endoscopy performed within 6 h and 97% within 24 h. The majority of patients with esophageal varices underwent EVL as the primary hemostasis modality, whereas cyanoacrylate glue was primarily used for patients with bleeding gastric varices (Table 4). Gastroenterologists performed endoscopy on 67% (n=54) of AVB patients, with the remainder being performed by general surgeons.

Use of pharmacological therapies

Octreotide: Octreotide was administered to 66 (82%) patients with AVB, 46 (70%) of whom received it before endoscopy. The mean duration of use of octreotide was 74.3±35.4 h. Univariate analysis did not identify a subgroup of patients who were more likely to receive octreotide.

Prophylactic antibiotics: Of 81 AVB patients, 20 (25%) either were previously using antibiotics for prophylaxis of spontaneous bacterial peritonitis, or were prescribed antibiotics on admission for a suspected or documented infection. Of the remaining 61 subjects eligible for antibiotic prophylaxis, 25% received appropriate treatment with either a fluoroquinolone or a third-generation cephalosporin. The prevalence of antibiotic use was significantly higher among patients with documented (clinical and/or radiological) ascites on admission versus those without ascites (P<0.001). Gastroenterologists were significantly more likely to recommend prophylactic antibiotics to AVB patients than were general surgeons (34% versus 9%, respectively, P<0.001). Furthermore, patients receiving prophylactic antibiotics had more severe underlying liver disease by MELD score than those who were not offered antibiotic prophylaxis (median MELD score 17 versus 14 respectively, P=0.04).

In multivariate analysis, the only variable that remained significant in predicting the use of prophylactic antibiotics was the presence of ascites (OR 22, 95% CI 4.3 to 114.8, P<0.001).

Beta-blocker prophylaxis: Sixty-six of 71 patients alive at the time of discharge did not have contraindications to beta-blockade, 16 (24%) of whom were discharged on a nonselective beta-blocker (nadolol or propranolol). In univariate analysis, the lower the MELD score and the more recent the year in which care was provided, the more likely it was that patients would receive prophylactic beta-blockers (OR 1.2, 95% CI 1.1 to 1.4, P=0.03 and OR 4.6, 95% CI 1.4 to 14.9, P=0.01, respectively). Patient age, etiology of cirrhosis, specialty of the initial consultant (gastroenterology versus general surgery), socioeconomic variables such as presence or absence of social support, smoking status, ongoing alcohol use and presence of comorbidities such as diabetes or congestive heart failure, were not predictive of a patient having received beta-blockers. Additionally, beta-blockers were as likely to be prescribed to individuals who had arrangements made for a subsequent follow-up endoscopy compared with individuals without arrangements for a follow-up endoscopy. In the multivariate analysis, the only factor that remained predictive of beta-blocker use was having received care in a more recent year.

Recommendations for postdischarge care

Recommendations for a follow-up endoscopy were made for 46 (65%) of 71 patients who survived the index hospitalization. A follow-up on discharge for the ongoing care of portal hypertension was arranged for 45% of patients with a gastroenterologist or a hepatologist (Figure 2).
performed in a timely fashion in patients with A VB, there
while endoscopy and endoscopic hemostasis were being
follow-up endoscopic therapies (8-13). Our study suggested that
therapy and to determine the requirements for performance of
postdischarge assessment to verify the response to ongoing
prophylactic antibiotics, and ensuring the proper arrangement of
pharmacological agents including octreotide, beta-blockers and
endoscopic hemostasis as indicated, use of adjuvant
management consists of performance of early endoscopy with
with signs and symptoms of A VB suggest that appropriate
care.

Outcomes
Hemostasis was achieved in 93% of endoscopies, and 71 (88%)
patients did not have evidence of rebleeding in the first 72 h
after performance of endoscopy. Ten (12%) patients died during
the index hospitalization. Older patients and patients with more
advanced liver disease with a higher MELD score had a higher
in-hospital mortality (P=0.05 and P<0.001, respectively). The
median length of hospital stay for patients admitted for A VB was
six days (range one to 66 days).

Of 71 patients who were discharged from the hospital
following their index episode of AVB, 25 (35%) patients were
readmitted for recurrent gastrointestinal bleeding within
six months. There were seven more confirmed deaths within
six months of hospital discharge among the 71 survivors of the
initial episode of variceal bleeding. Therefore, the overall
mortality rate at six months for patients presenting with A VB
was 21% (17 of 81 patient deaths). Regression analysis failed to
detect predictive factors for the outcomes.

DISCUSSION
Current guidelines concerning the care of patients presenting
with signs and symptoms of AVB suggest that appropriate
management consists of performance of early endoscopy with
endoscopic hemostasis as indicated, use of adjuvant
pharmaceutical agents including octreotide, beta-blockers and
prophylactic antibiotics, and ensuring the proper arrangement of
postdischarge assessment to verify the response to ongoing
therapy and to determine the requirements for performance of
follow-up endoscopic therapies (8-13). Our study suggested that
while endoscopy and endoscopic hemostasis were being
performed in a timely fashion in patients with AVB, there
remained substantial deficiencies in both the use of essential
nonendoscopic adjuvant therapies and the arrangement of
postdischarge medical care.

While numerous therapeutic modalities were previously used
for the performance of endoscopic hemostasis of acutely
bleeding esophageal varices, current data suggest that EVL is the
preferred technique, and should be followed by a continuous
infusion of intravenous octreotide (8,11,14-16). The use of EVL
is associated with lower rates of recurrent bleeding when
compared with endoscopic sclerotherapy, and has a decreased
risk of serious complications (16). The addition of octreotide to
endoscopic therapies is also associated with further decreases in
the rebleeding rate (14). Although we demonstrated that EVL
was used appropriately in the majority of patients, 20% of
patients did not receive adjunctive octreotide. Low rates of
concomitant vasoactive drug use (52.6% octreotide and
9.6% vasopressin) were also found in a recent American survey
(5). These rates compared poorly with those from a recent
practice review in a French study (6), where 90% of subjects
received adjunctive vasoactive therapy. Given the favourable
side effect profile of octreotide, there are few reasons which
justify its underutilization in our population.

Multiple studies and meta-analyses of published data (17-20)
have confirmed that providing prophylactic antibiotics to AVB
patients decreases both the risk of recurrent bleeding as well as
the overall mortality rate. Because antibiotics are generally well-
tolerated, they should have been provided to the overwhelming
majority of our study patients. Unfortunately, approximately
three-quarters of the eligible patients did not receive an
appropriate course of prophylactic antibiotics. Our data mirror
the findings of a study (21) performed at another Canadian
centre, that also reported similarly low rates of antibiotic use.
Although higher rates of prophylactic antibiotic use have been
reported in American and French studies (3,6), where antibiotic
use rates were 47% and 94%, respectively, use in less than
one-half of the patients in the American study should be
considered unsatisfactory. The higher rate of use of prophylactic
antibiotics in the French study was likely related to all of the
admissions and patient care being provided in a dedicated liver
care unit.

We determined that prophylactic antibiotics were more
likely to be used in patients with ascites and in those who were
assessed by a gastroenterologist as opposed to a general surgeon.
While antibiotics are often indicated in patients with ascites
because of suspicion of, or to prevent, spontaneous bacterial
peritonitis, other serious bacterial infections including urinary
tract infections, pneumonias and bacteremic episodes, frequently
occur in patients with cirrhosis and gastrointestinal bleeding and
are associated with an increased risk of rebleeding and mortality
(18). We believe that there is a need to improve clinician aware-
ness about the dangers of intercurrent infections and the need
for prophylactic antibiotics in cirrhotic patients with AVB.

The addition of beta-blockers to the performance of EVL is
effective for reducing the risk of recurrent AVB, and is therefore
recommended for all patients, without contraindications to
their use, undergoing variceal eradication with EVL once they
are hemodynamically stable (12,22,23). Unfortunately, we
determined that only 24% of eligible subjects were discharged
on beta-blockers, which was lower than the 46% to 81% rate of
use described in the recent American and French studies (3,5,6).
However, we did find that the prevalence of beta-blocker use
increased in recent years (4% in year 1, 27% in year 2 and 45%
in year 3 of the study). This is likely because the studies demonstrating the efficacy of adjunctive beta-blockers in patients undergoing EVL have been published only recently in the full form (23).

The arrangement of postdischarge medical care is also of paramount importance to fully realize the benefits of any endoscopic or pharmacological therapies which may have been initiated in the hospital. Most patients who undergo EVL for secondary prevention of AVB require multiple courses of endoscopic hemostasis to completely obliterate the culprit varices (16). If follow-up endoscopy is not performed after the performance of initial endoscopic hemostasis, the risk of recurrent AVB remains elevated, and may be as high as 60% to 80% over the following two years (2,24,25). Furthermore, patients who use beta-blockers require medical follow-up to assess patient compliance and to ensure users have had a satisfactory hemodynamic response. However, appropriate follow-up to manage portal hypertension and other complications of cirrhosis was arranged in only a minority of the patients in our study. This may reflect as an uncoordinated discharge planning mechanism for these patients in a busy tertiary care centre. It is also possible that we may have failed to capture the arrangement of postdischarge medical care if it was not explicitly written in the discharge summary.

Despite recent improvements in outcomes, variceal bleeding remains a highly fatal condition. Recent improvements in the outcomes of patients admitted with AVB are likely related to improvements in the various aspects of the process of care, including endoscopic and pharmacological therapies. It is disconcerting that strategies which have been proven to decrease mortality and morbidity are still underused at our centre. We believe that there are many possible explanations for the underutilization of these proven strategies. First, our centre does not use an organized care plan for subjects admitted with AVB. Therefore, there are no mechanisms to remind providers to perform all the necessary steps required to ensure the highest level of care for AVB patients. This likely explains why nongastroenterologists, who may be less likely to know all the components of quality care for AVB patients, are less likely to provide prophylactic antibiotics. Medical care plans have been shown to reduce the variation in the care provided, facilitate expected outcomes, reduce delays and reduce length of stay, and improve cost-effectiveness in the management of numerous other acute medical illnesses including acute myocardial infarction and nonvariceal gastrointestinal bleeding (26,27). Second, there are currently no published guidelines for the care of Canadian patients with AVB. Another Canadian study (21) also demonstrated low levels of prophylactic antibiotic use, suggesting that the deficiencies observed at our centre may exist nationwide. Guidelines have been proven to increase awareness regarding the proper management of a given condition, and the development of Canadian guidelines could lead to improvement in the care of AVB patients (28). Even though there are several guidelines from the United States national gastroenterology and endoscopy societies, there is a need for wider dissemination of existing guidelines as demonstrated by the limited use of appropriate care in several American studies (3,5,10,12). Establishment of dedicated liver care units or perhaps gastrointestinal bleeding units may further improve the process of care for patients with AVB, as suggested by the near-universal use of recommended care in the French study (6).

We would like to emphasize that gastroenterologists, hepatologists and endoscopists can be easily and rapidly accessed at our centre. Hence, there is ample opportunity to access experts in the practice of managing AVB. Yet we have still identified inadequacies in the management of AVB and suspect that these are common in other major centres that do not standardize management of this clinical problem. We believe that all hospitals should consider managing patients with AVB by establishing routine care maps so that each of the management steps that could improve outcomes in AVB is addressed.

One of the strengths of the methods in our study is the determination of the most comprehensive search strategy (ICD-9 codes) necessary for retrospectively identifying most patients with AVB. On the basis of chart reviews from the first year of the study, we were able to determine that by restricting the strategy to the specific ICD-9 codes for esophageal varices and varices of other sites (ICD-9 codes 456.0, 456.1, 456.2x and 456.8), we could still identify all patients with AVB. However, we would have missed some of the patients with AVB if we had not used all of the specific ICD-9 codes for esophageal varices and varices of other sites. Some of the other studies (4,21,29) have used limited search strategies and could have missed some of the patients admitted with AVB. It is unknown whether, although possible that, the lack of use of multiple discharge codes in retrospectively identifying patients with AVB may result in missing specific subpopulations of patients with AVB who may be managed differently and may have different clinical outcomes than those identified using the ICD-9 code, or ICD-10 code that is specific for bleeding esophageal varices.

Beyond the retrospective design, other limitations of our study include the computation of the six-month rebleeding and mortality rates based on readmissions to our centre because some of the patients may have been readmitted and/or died at another hospital. Therefore, we may have underestimated the true rebleeding and mortality rates for subjects in our study. However, most of the patients with AVB in Manitoba are ultimately transferred to our study centre, which is the largest tertiary care hospital in the province. Another limitation of our study is the evaluation of a single centre experience, which therefore has perhaps limited generalizability to other centres. However, low rates of beta-blocker and prophylactic antibiotic use were also found in the only other published Canadian study (21,29).

CONCLUSIONS
Although there exist strategies that are proven effective to improve the outcome of patients with AVB, the uptake of these practices with the exception of performance of initial endoscopic hemostasis has been limited. Several deficiencies were identified in our study, most notably the low use of both prophylactic antibiotics and beta-blockers, and suboptimal arrangement of postdischarge care. Measures to improve the process of care provided to patients with AVB need to be developed to ensure that the highest quality of care is offered to these patients.

The current study was presented in part at the Digestive Disease Week, Chicago, USA, on May 15, 2005, and the World Congress of Gastroenterology, Montreal, Quebec, on September 14, 2005.
REFERENCES


