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Introduction

Bleeding from esophageal or gastric varices is a life-threatening complication of cirrhosis, and the endoscopic appearance of the varices has been shown to be predictive of bleeding risk. Screening is based on upper endoscopy, and current guidelines recommended a screening endoscopy be performed on all cirrhotics to document the presence or absence of varices and to define therapy [1]. However, as technology has advanced, a number of tests, from the simple CBC to new technologies such as elastography, have been proposed as the best way to screen for varices [2]. The difficulty with all of the reports on the new approaches to the diagnosis of portal hypertension is the lack of a common end point. When using endoscopy, the most important end point is the finding of high-risk varices. In contrast, in most studies which use noninvasive tests, the end point has been the presence of varices irrespective of size or clinically significant portal hypertension with or without varices. One can question whether or not this is appropriate as it is the large varices with or without red signs that are associated with the greatest risk of bleeding and are the current targets of treatment [1]. How to manage those with small varices or with portal hypertension without varices is unclear given the uncertain benefit from beta blockers on variceal growth and risk of bleeding [3, 4]. The purpose of this review is to look at cost and see if it should be a factor in determining how we screen for varices. The relative costs of each screening test are shown in Table 8.1.

The first question is whether or not screening is even necessary. Perhaps the best approach would be to place all patients with cirrhosis on beta blockers given their proven efficacy in reducing the risk of bleeding. This approach has been examined

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Table 8.1 Relative cost of tests used to screen for varices

Test	Relative cost (least to most)
Platelet count	+
Ultrasound	+++
Elastography	++++
CT scan	+++++
Upper endoscopy	+++++
Pill endoscopy	++++
WHVP	+++++

in two separate reports using Markov modeling. Firstly, not screening or treating was an unacceptable option as it was not expensive or effective. Placing all patients on beta blockers was the most cost-effective approach with an incremental cost of \$12,408 per additional variceal bleed prevented. Adding screening endoscopy with a beta blocker or variceal band ligation (VBL) to follow added ~\$170,000 to the cost of preventing a variceal bleed [5]. The analysis also suggested that using pre-screening tests, such as platelet counts or splenomegaly, was not cost-effective as well. In a second report looking at cost/life saved, universal screening was the most cost-effective in compensated cirrhotics, but in decompensated cirrhotics, primary prophylaxis without screening was the most cost-effective [6]. For all of these studies, the incidence of large varices in the patient population and cost of drugs and upper endoscopy affected the results of the modeling. Other important factors that make the treat all approach less appealing include the fact that the incidence of varices in cirrhotic populations is quite variable and perhaps only 12–20 % will have high-risk varices which is the target population. Also, 70 % of patients will have no varices [6–8]. Beta blockers also cause a clinically significant fall in the hepatic venous pressure gradient (HVPG) in ~50 % of patients [9, 10] leaving the other 50 % at risk for bleeding. Thus, if one treats 100 cirrhotics with beta blockers, the 65 patients with no varices will have no benefit. The 20 patients with small varices may or may not have a benefit [3, 4]. Thus, only 7 of the 15 with large varices will have a therapeutic benefit from treatment. That is not an acceptable number considering the side effects of beta-blocker therapy. We need better noninvasive tests to help direct who should be screened for varices in a cost-effective manner.

Instead of the treat all or scope all strategy, we need to define the population at risk for having high-risk varices or variceal progression in order to improve the cost-effectiveness of our approach. One approach is to screen all patients initially placing those with high-risk varices on beta blockers. In addition, those with small varices can be placed on a beta blocker as well. This approach was modeled using variceal progression, bleeding, and death as a composite end point. Treating those with small varices with beta blockers was more cost-effective as compared to repeated screening endoscopies waiting for the varices to grow before initiating treatment [11].

The least expensive approach is the use of the platelet count in combination with the size of the spleen. Using the platelet count alone or the spleen diameter/platelet count ratio (SDPC) has a modest sensitivity (0.8) in identifying clinically significant portal hypertension (CSPH-HVPG ≥ 10 mmHg) and/or varices.

Somewhat more expensive is measuring liver stiffness (LS) which is more sensitive than the platelet count/spleen diameter in identifying patients with varices. When LS and SDPC are combined, the sensitivity approaches 0.9 for the diagnosis of varices and in one report the negative predictive value for high-risk varices was almost 100 % [2, 7]

Based on the above data, if upper endoscopy was only performed on those with CSPH, 54 % would have no varices, 28 % small varices, and 18 % large varices. In those not reaching the screening threshold, only 2.5 % would have varices, none of which would be large [7]. Thus, one could reduce the number of patients with cirrhosis who need screening. Could this selective approach be cost-effective? In one report platelet counts of <88,000 or the presence of splenomegaly were associated with the presence of large varices. The incremental cost of averting each variceal bleed was \$3533 for the selective approach (endoscopy only those with low platelet counts or splenomegaly) and \$15,160 for the scope all approach. The risk of large varices in those lacking either risk factor was 7.2 %. However, the difference in the predicted number of variceal bleeds between the two groups was small, 12.9 vs. 12.4, for selective versus scope all strategy, respectively [8]. These studies suggest that we should be more selective in the patients we screen for varices. Establishing thresholds of platelet counts and presence or absence of splenomegaly as indications for screening endoscopy would reduce the number of endoscopies performed, improve the benefits of screening endoscopy, and most likely save money as well.

One alternative to endoscopy is using the computed tomography (CT) scan to detect varices. In one series screening with CT and treating those patients with large varices with beta blockers was more cost-effective than was screening endoscopy. The cost using CT to screen was \$232 to prevent one variceal bleed vs. \$35,000 using screening endoscopy to prevent one variceal bleed [12]. When screening with CT vs. endoscopy was compared in a managed care environment using modeling, CT was again more cost-effective [13]. Ultrasound (US) has also been used to screen for varices. The finding of increased thickness of the esophageal wall is associated with the presence of varices but the cost-effectiveness of this approach is unknown [14]. Lastly, is the performance of PillCam esophagoscopy more cost-effective than EGD to screen for varices? Using Markov modeling PillCam was more cost-effective, but the results were influenced by the ability of PillCam to distinguish between large and small varices as well as cost and prevalence of large varices. The authors concluded that they are equivalent strategies based on cost [15].

In conclusion, although giving beta blockers to all cirrhotics may be cost-effective in the prevention of variceal bleeding, it is not clinically practical to take this approach. Alternatively, the scope all strategy also is not practical as it is the most costly approach for variceal screening. Clearly using noninvasive tests allows for the prediction of which cirrhotics are and perhaps more importantly are not at risk for varices [7]. In a limited number of studies, these noninvasive tests are more cost-effective than screening endoscopy as discussed above. We need to develop cost-sensitive recommendations about which patients need endoscopic screening for varices.

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