

SHOULD CONCERN OVER GASTRIC CANCER INFLUENCE
THE CHOICE OF DIAGNOSTIC TESTS IN PATIENTS WITH
ACUTE UPPER GASTROINTESTINAL BLEEDING?

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ABSTRACT

Despite data from well designed clinical trials showing no benefit in patient outcome, most physicians obtain diagnostic endoscopy to determine the site of bleeding on all patients with acute bleeding from the upper gastrointestinal tract. The purpose of this study was to determine whether concern over a possible bleeding stomach cancer, an uncommon cause of acute upper gastrointestinal hemorrhage, is sufficient reason to justify a policy of routine endoscopy for the 50% of patients who can be identified as having a low risk for a poor outcome.

The analytic hierarchy process (AHP) was used. The decision hierarchy contained two scenarios, malignant bleeding and non-malignant bleeding. Under each scenario there were four objectives - avoid complications of bleeding, avoid test complications, identify the bleeding site, and minimize cost - and three alternatives: routine endoscopy, routine upper gastrointestinal X-rays, and no routine diagnostic tests.

The analysis revealed that judgments under the malignant scenario did not affect the choice of diagnostic strategy which was wholly determined by judgments under the non-malignant scenario. This finding indicates that concern over malignancy should not influence the diagnostic approach to low risk patients with acute upper gastrointestinal bleeding. The best diagnostic approach depends on the relative importance of management objectives in patients with bleeding due to non-malignant causes.

INTRODUCTION

Acute bleeding from the upper gastrointestinal (GI) tract is a common medical problem which accounts for approximately 300,000 hospital admissions annually in the United States. [1] Although most patients recover uneventfully, upper GI bleeding is a serious disease with a mortality rate between 5% and 10%.

Most bleeding is caused by three diseases of the upper gastrointestinal tract: peptic ulcer disease, acute gastritis, and esophageal varices. Peptic ulcer disease results in the formation of an ulcer in the wall of the stomach or duodenum (the first part of the small intestine just beyond the stomach). Although the exact cause of peptic ulcer disease is unknown, the acid normally produced by the stomach plays a major role in ulcer formation. Bleeding occurs if a blood vessel is damaged as the ulcer enlarges. Acute gastritis refers to a diffuse irritation of the lining of the stomach. Common causes of gastritis are some medicines, alcohol, and severe illness. If the irritation is severe enough, blood vessels in the wall of the stomach can be damaged and bleed. Esophageal varices are engorged veins in the wall of the esophagus caused by partial obstruction of blood flow through a chronically diseased liver. Bleeding occurs when the varices rupture due to elevated pressure inside the vessel.

Standard treatment for acute bleeding from all three conditions includes blood and fluid replacement and medicines intended to decrease the production of acid in the stomach or to protect the stomach from the acid. In most cases of bleeding due to

gastritis or peptic ulcer disease, the hemorrhage stops and no additional therapy is needed. Occasionally, however, further measures, such as surgery or treatment through an endoscope, are needed to control the bleeding. Both gastritis and peptic ulcers tend to be self-limited processes and resolve over 6 to 8 weeks, although recurrences sometimes develop.

Acute bleeding due to esophageal varices is more difficult to treat and, because the varices themselves persist, patients with hemorrhage due to esophageal varices have a good chance of having subsequent bleeding episodes. For these reasons, variceal bleeding is routinely treated with additional measures to stop the acute hemorrhage and prevent future hemorrhage.

There are several other less common problems which cause bleeding, most of which are self-limited and treated in a fashion similar to gastritis and peptic ulcer disease. The single major exception is bleeding due to stomach cancer. In large series hemorrhage due to cancer accounts for about 3% of all acute bleeding episodes. [2][3] Stomach cancer is fatal without treatment, and once diagnosed requires further investigation to determine whether curative surgery is possible. Unfortunately, by the time a cancer has advanced far enough to cause an episode of acute bleeding, most patients have incurable disease.

In addition to the treatment measures mentioned above, it has become standard practice to routinely perform diagnostic endoscopy on patients who have upper GI bleeding. An endoscope is a flexible fiberoptic instrument that is passed through the mouth into the patient's stomach and duodenum. Looking through the instrument, the endoscopist can directly visualize the inside of the upper gastrointestinal tract and in most cases identify the source of bleeding.

When the flexible endoscope was first introduced, it was hoped that knowledge of the bleeding site would improve the outcome of patients with acute upper GI bleeding and it soon became a routine procedure. However, in randomized controlled trials there have been no differences in outcome between patients who are routinely endoscoped soon after they arrive at the hospital and those who have an X-ray taken of their upper GI tract several days later. [4][5] Despite this failure to document benefit, the majority of patients with acute upper GI bleeding continue to be endoscoped.

The customary reason for obtaining diagnostic information is to guide patient management. In the treatment of acute upper GI bleeding, management is the same for all causes of bleeding except esophageal varices and stomach cancer. Since studies have demonstrated that most patients with esophageal varices can be identified on clinical grounds prior to endoscopy, [2][6] significant changes in management after endoscopy are likely only for patients with cancer.

In this study we used the analytic hierarchy process (AHP) to determine whether the incidence of bleeding stomach cancer is high enough to justify routine endoscopy for all patients presenting to the hospital with acute upper GI bleeding.

METHODS

PATIENT POPULATION. We limited our analysis to adult patients presenting to a hospital with a documented episode of acute upper gastrointestinal bleeding who meet previously defined criteria for low risk of a poor outcome from their bleeding event. [7] In addition to defining a low risk population, these criteria also exclude most patients with bleeding esophageal varices. We also excluded patients who have had abdominal vascular surgery in whom upper GI bleeding can represent a complication of their surgical procedure. We included only patients who respond to routine management, are stable four hours after arrival in the hospital, and do not have recurrent bleeding during their hospitalization. All patients who rebleed are immediately considered to be at high risk for a poor outcome and excluded from our target patient population. (The importance of delineating the cause of bleeding through diagnostic endoscopy in high risk patients, many of whom require surgery to control the bleeding, has been clearly shown. [8])

THE DECISION MODEL. The hierarchy we used for the analysis is shown in Figure 1. Under the overall goal of choosing the best management, we define two scenarios: malignant bleeding from a stomach cancer and non-malignant bleeding. For each scenario, there are four management criteria - avoid complications of bleeding, avoid test complications, identify the bleeding site, and minimize the cost of the diagnostic workup - and three alternative management strategies: routine endoscopy, upper GI series and no test.

DEFINITIONS OF ALTERNATIVE MANAGEMENT STRATEGIES.

The endoscopy procedure was described earlier. The routine endoscopy strategy refers to obtaining endoscopy on all patients. This is the most popular strategy in current practice.

An upper GI series is an X-Ray study of the upper gastrointestinal tract. Before fiberoptic endoscopes were developed, an upper GI series was the best diagnostic test available to delineate the cause of upper GI bleeding. It is still considered a reasonable strategy; in most scientific trials of endoscopy in upper GI bleeding the control groups have had upper GI series obtained instead of endoscopy.

The strategy of obtaining no diagnostic test to delineate the cause of bleeding has never been compared to either of the other strategies in a clinical trial. We included it in our analysis because the data resulting from the studies comparing endoscopy with upper GI series suggest that no test may be an appropriate strategy for many patients.

DECISION CRITERIA: DEFINITIONS AND DATA.

AVOID BLEEDING COMPLICATIONS. The major complications of bleeding from non-malignant causes are death or permanent injury due to

acute blood loss. Most physicians also consider recurrent episodes of bleeding and the need to have urgent surgery to stop the hemorrhage complications of a bleeding episode. There is no evidence that the frequency of these complications is decreased by any of the three diagnostic strategies under either scenario. [9][10] We therefore considered all three strategies equivalent with respect to this criterion.

AVOID TEST COMPLICATIONS. Diagnostic endoscopy is generally considered a safe test. A large multicenter study sponsored by the American Society of Gastrointestinal Endoscopists revealed that the frequency of major complications of endoscopy done in acutely bleeding patients is about 5 per 1,000, including 1 death. [11] Since there is no reason to suspect that the rate of complications would be affected by a malignant source of bleeding, we used the same complication rate for both scenarios in the analysis.

IDENTIFY THE BLEEDING SITE. Endoscopy is clearly the best of the three strategies in identifying the bleeding site. If done within 24 hours of onset, diagnostic endoscopy has been shown to correctly identify about 90% of all bleeding lesions with very few false positive results. Its reported sensitivity and specificity are approximately 90% and 95%. [12][13][14]

Upper GI series, on the other hand, is much less sensitive if all acutely bleeding lesions are taken together (sensitivity 60%) though it is about equal to endoscopy in avoiding false positive results (specificity 90-95%) [13][14][15][16] The upper GI series may be more sensitive for the diagnosis of gastric cancer, with a sensitivity of about 80%.

The No Test strategy gives no information beyond the baseline prevalence rate regarding the source of bleeding. We therefore equated this strategy with a non-informative diagnostic test with both sensitivity and specificity equal to 50%.

Comparisons among the three strategies relative to identifying the source of bleeding were done using their positive likelihood ratios which indicate how much the odds of disease are increased following a positive test result. The likelihood ratios were calculated by dividing test sensitivity by (1-specificity).

MINIMIZE COST. For our analysis we considered only the direct cost of the diagnostic tests included in each strategy which we estimated to be \$600 for endoscopy, \$175 for upper GI series, and \$0 for no test. These estimates were based on current charges in Rochester, New York.

PAIRWISE COMPARISONS

ALTERNATIVES RELATIVE TO DECISION CRITERIA

Table 1 summarizes the data used to compare the three alternatives relative to avoiding test complications, identifying the bleeding site, and minimizing cost. As noted above, the

alternatives were considered equal with regard to avoiding complications of bleeding. For our baseline analysis pairwise comparisons were made by the authors using standard AHP methodology. The results are shown in Table 2.

CRITERIA RELATIVE TO SCENARIO.

We made comparisons among the criteria under each scenario according to the series of perspectives listed in Table 3. These combinations were chosen to cover the spectrum of clinically realistic points of view. Four different points of view were chosen for the non-malignant scenario and three for the malignant scenario. We first calculated the best strategy for each of the four points of view using just the non-malignant scenario. We then determined the importance of the considerations included under the malignant scenario by recalculating the results when each of the three points of view under the malignant scenario are included in the analysis.

MALIGNANT BLEEDING VERSUS NON-MALIGNANT BLEEDING.

In large series of patients with acute upper GI bleeding, the frequency of stomach cancers has been between 2.5% and 3%. [2][3] Recurrent bleeding after initial stabilization occurs in about 50% of patients with bleeding due to malignancy. [2] Using these data, we estimated that the prevalence of bleeding stomach cancers in our low risk patient population was about 1.5% ($3\% \times 0.5$) with an upper limit of 5%. For our baseline analysis we used weights of 0.985 and 0.015 for the non-malignant and malignant scenarios respectively. All calculations were repeated after changing the prevalence of malignant bleeding to 0.05.

COMPUTATIONAL METHOD. All analyses were done using Expert Choice. [17]

RESULTS

The results of the baseline analysis are shown in Figures 2A-D.

Figure 2A displays the situation from point of view A, where all management criteria are considered equal under the non-malignant scenario. Using just the non-malignant portion of the hierarchy, labeled as point of view 0 in the figure, the most preferred strategy is No Test with a weight of 0.384; Endoscopy is the second best strategy with a weight of 0.316. The analyses labeled as points of view 1 to 3 indicate that including the malignant scenario in the analysis does not affect the results: for every point of view adopted under the malignant scenario the result is the same as when the malignant scenario is completely disregarded.

Figures 2B-D illustrate that this result is the same for all four points of view under the non-malignant scenario that we studied. This finding also did not change if either the relative strengths of preference among the criteria or the strengths of

preference among the alternatives relative to the criteria were varied from slight to extreme. Similarly, increasing the prevalence of malignancy to 0.05 did not affect the results.

DISCUSSION

These findings indicate that concern over a possible bleeding stomach cancer should not be used to justify the routine use of diagnostic endoscopy in patients meeting the criteria for a low risk of a poor outcome from an episode of upper GI bleeding. As shown in Figures 2A-D, the small possibility of a bleeding stomach cancer does not affect the choice of patient management. Rather, the best strategy depends on the relative importance given to the management criteria in the non-malignant scenario.

For three of the four points of view studied, no routine diagnostic test was the preferred strategy. This finding suggests that this strategy should be considered more often in the management of patients with acute upper GI bleeding.

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17. Expert Choice. Copyright Expert Choice Inc. Pittsburgh PA.

Table 1. Data comparing alternatives and criteria.

Alternative	Avoid Bleeding Complications	Avoid Test Complications	Identify the Bleeding Site		Minimize Cost
			Non-Malignant	Malignant	
Endoscopy	Equal	0.005	18	18	\$600
Upper GI Series	Equal	0	6	8	\$175
No Test	Equal	0	1	1	\$0

* - Data regarding this criterion are expressed in terms of each strategy's positive likelihood ratio defined as test sensitivity - (1 - specificity).

Table 2. Comparison matrices for each strategy relative to avoiding test complications, minimizing costs and identifying the bleeding site.

A. Avoid Test Complications (Both Scenarios)

	E	UGI	NT	Priority
Endoscopy (E)	1	1/4	1/4	.111
Upper GI series (UGI)	4	1	1	.444
No Test (NT)	4	1	1	.444

Consistency ratio = 0.00

B. Minimize Cost (Both Scenarios)

	E	UGI	NT	Priority
Endoscopy (E)	1	1/4	1/7	.075
Upper GI series (UGI)	4	1	1/4	.229
No Test (NT)	7	4	1	.696

Consistency ratio = 0.073

C. Identify the Bleeding Site (Non-Malignant Scenario)

	E	UGI	NT	Priority
Endoscopy (E)	1	5	9	.743
Upper GI series (UGI)	1/5	1	4	.194
No Test (NT)	1/9	1/4	1	.063

Consistency ratio = 0.068

D. Identify the Bleeding Site (Malignant Scenario)

	E	UGI	NT	Priority
Endoscopy (E)	1	4	9	.709
Upper GI series (UGI)	1/4	1	5	.231
No Test (NT)	1/9	1/5	1	.060

Consistency ratio = 0.068

Table 3. Different points of view regarding comparisons among decision criteria.

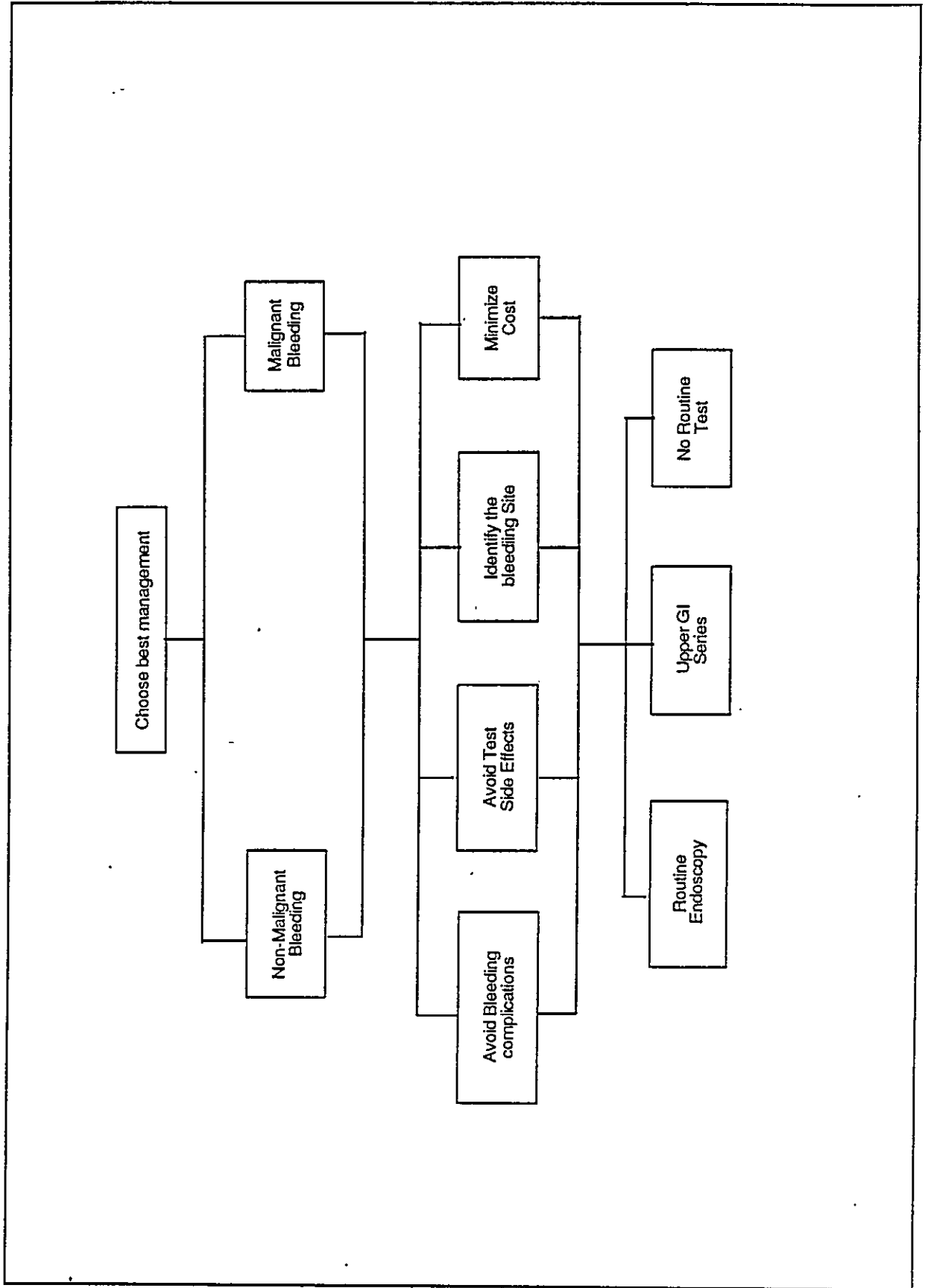
NON-MALIGNANT SCENARIO

- A. All criteria are equally important
- B. Avoiding complications of bleeding, identifying the bleeding site, and avoiding test complications are strongly more important than minimizing cost.
- C. Avoiding complications of bleeding and avoiding test complications are strongly more important than identifying the bleeding site or minimizing cost.
- D. Avoiding complications of bleeding, avoiding test complications and minimizing cost are moderately more important than identifying the bleeding site.

MALIGNANT SCENARIO

- 1. All criteria are equally important.
- 2. Avoiding complications of bleeding, identifying the bleeding site, and avoiding test complications are strongly more important than minimizing cost.
- 3. Avoiding complications of bleeding and identifying the bleeding site are moderately to strongly more important than avoiding test complications and minimizing cost.

Figure 1. The decision hierarchy.



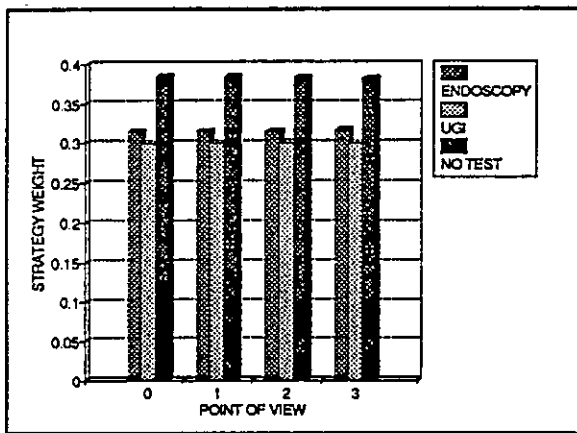


Figure 2A.

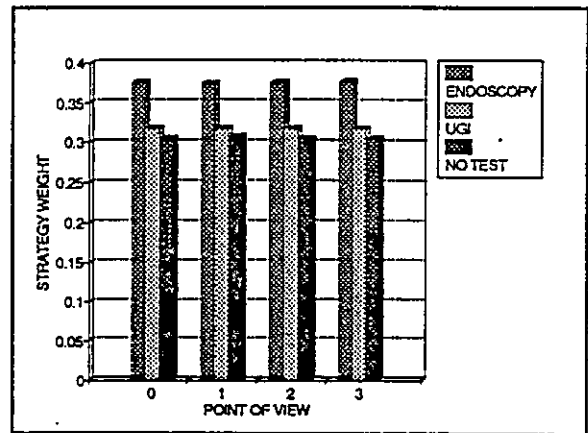


Figure 2B.

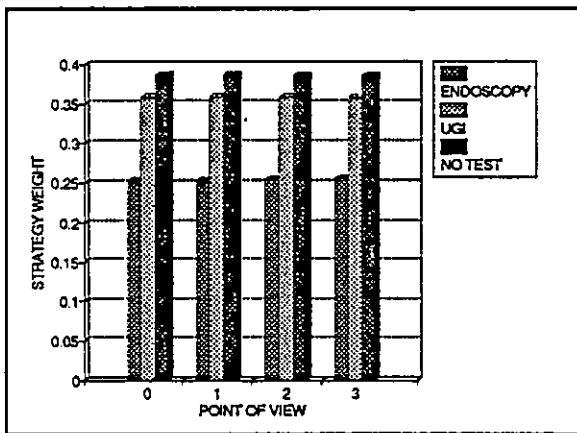


Figure 2C.

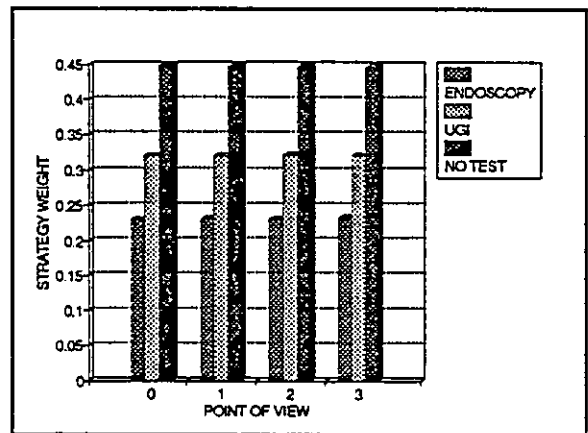


Figure 2D.

Figure 2A-D. In each case the left hand bars represent the endoscopy strategy, the middle bars represent the upper GI strategy, and the right hand bars represent the no test strategy. Strategy weight equals overall priority weight given to each strategy. Figures A-D represent the results using the corresponding point of view for the non-malignant scenario defined in Table 3. Point of view 0 indicates the results of the analysis using only the non-malignant scenario. Points of view 1 to 3 indicate the results when the malignant scenario using the corresponding point of view defined in Table 3 are included in the analysis.