Costs of Treating Bleeding and Perforated Peptic Ulcers in The Netherlands

HELENA T.J.I. DE LEEST, HISKE E.M. VAN DIETEN, MAURITS W. VAN TULDER, WILLEM F. LEMS, BEN A.C. DIJKMANS, and MAARTEN BOERS

ABSTRACT. ***Objective.*** Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs includes perforations and bleeds. Several preventive strategies are being tested for cost-effectiveness, but little is known about the costs of the complications they are trying to prevent. We estimated the direct costs of hospital treatment of bleeding and perforated ulcers in a university hospital, from data in discharge letters and the hospital management information system.

Methods. Eligible patients had been treated in the VU University Medical Center between January 1997 and August 2000 for an ulcer bleed or perforation (*International Classification of Diseases* code 531–4). Resource use comprised hospitalization days and diagnostic and therapeutic interventions. Insurance claim prices determined the costs from the payers' perspective. In a secondary analysis we excluded resource use that was clearly related to the treatment of comorbid illness.

Results. Fifty-three patients with a bleeding (n = 35) or perforated ulcer (n = 15) or both (n = 3) were studied, including 14 with comorbidity; 22 complications occurred in the stomach, 29 in the duodenum, one in both stomach and duodenum, and one after partial gastrectomy. A simultaneous bleed and perforation was most expensive (€ 26,000), followed by perforation (€19,000) and bleeding (€12,000). A bleed in the duodenum was more expensive than in the stomach (€ 13,000 vs € 10,000), while the opposite was seen for perforations (€ 13,000 vs € 21,000). Comorbidity increased costs substantially: even after correction for procedures unrelated to the ulcer complication, comorbidity more than doubled the costs of treatment.

Conclusion. Treatment of complicated ulcers is expensive, especially in patients with comorbid conditions. (J Rheumatol 2004;31:788–91)

Key Indexing Terms:
COSTS
COST ANALYSIS
PEPTIC ULCER PERFORATION
PEPTIC ULCER HEMORRHAGE

Peptic ulcers of the upper gastrointestinal (GI) tract are a frequent side effect of nonsteroidal antiinflammatory drugs (NSAID). Although most ulcers are asymptomatic and heal without therapy, a small proportion causes potentially life-threatening bleeding and perforation[1]. The annual incidence of gastropathy among chronic NSAID users varies from 15% to 20% for mild events[2] and 1–2% for serious events such as hemorrhage and perforation[3-5]. Several factors such as age and a history of peptic ulcers can substantially increase this risk.

Treatment of ulcer complications is relatively standard, but little is known about their costs in The Netherlands. Bleeding ulcers are most frequently treated by endoscopic injection of adrenaline. To prevent early recurrences this is often followed by clipping of the blood vessel[6]. Perforated ulcers are treated operatively by suture repair or with fibrin glue either by laparotomy or by laparoscopy[7].

Several strategies are being tested to prevent NSAID-induced gastropathy. These include medical cotherapy with high dose histamine-2 receptor blockers, proton pump inhibitors or misoprostol, or replacement of NSAID by cyclooxygenase-2 (COX-2) selective antagonists. When proven effective, implementation of any of these would have important economic consequences. In September 1999 we started a randomized controlled trial on the effectiveness of *Helicobacter pylori* eradication in the prevention of NSAID-induced gastropathy. A parallel cost-effectiveness analysis is under way. Because of the low incidence of bleeding and perforations, it is not possible to reliably calculate the cost of treatment of these complications within this trial.

Thus, we conducted a retrospective study to estimate the direct hospital costs of treatment of upper GI bleeding and perforation from the payer perspective.

MATERIALS AND METHODS

With the eligibility criteria of the trial in mind, patients aged between 39 and 80 years with a gastric or duodenal ulcer complicated by bleeding or

From the Department of Clinical Epidemiology and Biostatistics and the Department of Rheumatology, VU University Medical Center, Amsterdam, The Netherlands.

H.T.J.I. de Leest, MD; W.F. Lems, MD, PhD; B.A.C. Dijkmans, MD, PhD, Department of Rheumatology; H.E.M. van Dieten, MSc; M.W. van Tulder, PhD; M. Boers, MD, PhD, Department of Clinical Epidemiology and Biostatistics.

Address reprint requests to Dr. H. de Leest, VU University Medical Center, PO Box 7057, Room 4A42, 1007 MB Amsterdam, The Netherlands. E-mail: M.deleest@vumc.nl

Submitted November 21, 2002; revision accepted October 20, 2003.

Personal, non-commercial use only. The Journal of Rheumatology Copyright © 2004. All rights reserved.

Downloaded on April 24, 2024 from www.jrheum.org

perforation (*International Classification of Diseases* codes 531, 532, 533, and 534) treated in the VU University Medical Center (VUMC), Amsterdam, between January 1997 and August 2000 were selected. Patients transferred to or from other hospitals in the course of their admission were excluded because the data for these patients would be incomplete. On the basis of the discharge letters 3 authors (HvD, MB, and WL) independently selected the patients for inclusion in the study; conflicts were resolved by consensus. Only patients with ulcer bleeds and perforations that were confirmed by endoscopy, surgery, or autopsy were included.

The VUMC management information system (COGNOS) yielded the following data per patient: (1) demographic data (age, sex); (2) number of days hospitalized (normal care, special care, or intensive care); and (3) diagnostic and therapeutic interventions (e.g., radiodiagnostic tests, blood products used, laboratory tests, and surgical procedures).

Costs of hospitalization days were estimated using the charges claimed at the patients' health insurance companies. Costs of medication are included in these charges and were not estimated separately. The costs of radiodiagnostic tests summarized as "specific" and "general" are charges computed by the medical administration of the VUMC. Specific radiodiagnostic tests comprise computed tomography (CT), magnetic resonance imaging, and angiography. General radiodiagnostic tests include all other procedures with or without contrast and ultrasound procedures. Costs paid to the supplier of blood products listed in the VUMC information system were used to estimate the costs of blood products. The costs of tests necessary before infusion of blood products were not incorporated. The costs of laboratory tests per patient consist of a general charge for the test, personnel costs, costs of materials and costs of equipment. The costs of diagnostic and therapeutic interventions (e.g., endoscopies, endoscopic injection, laparotomy, laparoscopy) were also estimated using the insurance claim charges.

The total costs of treating bleeding and perforated ulcers were calculated by adding the costs of all components.

Preexisting comorbidity likely results in prolonged hospitalization or extra treatment that may be unrelated to treatment of the bleeding or perforated ulcer. In a secondary analysis, distinction was therefore made between costs of patients without comorbidity, patients with comorbidity, and patients with comorbidity corrected for procedures and hospitalization days not related to the treatment of the bleeding or perforated ulcer. To determine the influence of comorbidity on the costs of treatment, significant costs that could be directly linked to preexisting comorbidity, independent of the ulcer complication, were extracted. Although of necessity an arbitrary procedure, MB and WL independently checked the cases with comorbidity and resolved discrepancies in consensus. The criteria to exclude procedures/costs were: (1) the procedure clearly antedated the ulcer complication, or (2) it was completely evident that the procedure was unrelated to the ulcer complication, and (3) the procedure or package of procedures was inexpensive (< € 90).

To illustrate this procedure 2 examples are given:

1. A patient was admitted with melena after taking NSAID for severe back pain. She died in hospital after 10 days of intensive care due to septic shock. In reconstruction, alcohol abuse had resulted in liver cirrhosis and a poor general condition. She developed staphylococcal endocarditis and spondylodiscitis followed by sepsis. The discitis prompted the use of NSAID, which led to multiple gastric and duodenal ulcers from which she bled. Multiple organ failure developed despite optimal therapy. Costs of care included a variety of expensive diagnostic tests (e.g., multiple CT scans of brain and abdomen), hemodialysis, and autopsy. In this case we were unable to exclude any costs as "unrelated to the ulcer bleeding."
2. Another patient was admitted to the department of surgery for arterial insufficiency of the right leg. He died after 28 days. His history included complicated arteriosclerosis with an aneurysm of the aorta treated with a vascular prosthesis and dialysis-dependent renal failure. After angiography his condition worsened, necessitating an acute laparotomy. A total obstruction of the femoral artery could be reversed, but the leg had suffered too much ischemic damage and had to be amputated. Four days after surgery an acute abdomen developed. A re-laparotomy revealed perforated ulcus ventriculi that was closed. The postoperative course was complicated by progressive heart failure, to which the patient succumbed. In this case we decided to exclude in the secondary analysis as "unrelated" all costs related to the first surgical procedures, the vascular investigations, and the hemodialyses.

Unless stated otherwise all costs are expressed in Euros; 1 Euro (€) = 1.14 US$.

RESULTS

In the selected period 164 patients were admitted to the VUMC with the specified ICD codes 531–534. Of these, 97 were between 39 and 80 years of age. Twenty-one patients were transferred to or from other hospitals and 23 patients were incorrectly classified, i.e., the admission did not concern bleeding or perforation of a peptic ulcer. Thus, 53 patients were finally included. Fourteen of these patients had severe comorbidity, such as diabetes mellitus, cardiovascular diseases, and neurological disorders. Mean age was 63 years with a slight male predominance (Table 1). On admission, 37 patients were treated with antisecretory agents, usually proton pump inhibitors.

Events included 35 bleeds, 15 perforations, and 3 occurrences of both complications. Twenty-two patients had complications in the stomach, 29 in the duodenum. Of the 2 remaining cases, one had multiple bleeding ulcers in both stomach and duodenum and the other had a bleeding ulcer on the anastomosis of a previous Billroth II gastrectomy (Table 1).

Routine diagnostic interventions (chest radiograph, blood hemoglobin levels) were by far the most frequent procedures. Suture repair of perforations and bleeding vessels were the most frequent therapeutic interventions. Table 2 shows the costs of the frequently used, complication-related interventions and hospitalization days.

Overall, treatment of a simultaneous bleeding and perforated ulcer costs € 26,000, treatment of a perforated ulcer € 19,200, and a bleeding ulcer € 11,900. For all types of complications the costs of hospitalization days were the greatest part of the total costs. In the subgroup of patients with comorbidity, cost of treatment was substantially higher: perforation € 38,000 and bleeding € 25,200. Adjustment for procedures unrelated to the treatment of the ulcer complication partially corrected this difference, mostly due to lower costs of interventions (Table 3). In the stomach, ulcer bleeds were less costly than in the duodenum (€ 9,600 vs € 13,000), but perforations were more costly (€ 21,500 vs € 13,100; Table 3).

DISCUSSION

We estimated the direct hospital costs of treatment of bleeding and perforated ulcers in our university hospital. Direct costs of treatment of ulcer complications were high, especially in patients with comorbidity. Even after correction for procedures unrelated to the ulcer complication, costs of treating patients with comorbidity remained more than twice the cost for patients without comorbidity.

Personal, non-commercial use only. The Journal of Rheumatology Copyright © 2004. All rights reserved.

Downloaded on April 24, 2024 from www.jrheum.org

Table 1. Patient characteristics by comorbidity status.

	All Patients, n = 53			Patients without Comorbidity, n = 39			Patients with Comorbidity, n = 14		
Male, %	66			67			64		
Age, yrs, mean (SD)	63 (12)			62 (12)			66 (11)		
Event	Bleeding	Perforation	Both	Bleeding	Perforation	Both	Bleeding	Perforation	Both
Ulcus ventriculi	10	11	1	8	8	1	2	3	0
Ulcus duodeni	23	4	2	16	4	2	7	0	0
Use of antisecretory agents (%)	37 (70)			30 (77)			7 (50)		
Total hospitalization days, mean (SD)	8.7 (7.9)			8.7 (8.5)			8.9 (6.5)		
Normal care days	7.5 (8.1)			8.1 (8.4)			5.7 (7.1)		
Special care days	0.2 (0.6)			0.1 (0.5)			0.4 (0.9)		
Intensive care days	1.2 (2.7)			0.5 (2.1)			2.9 (3.5)		

Two patients could not be unequivocally classified: one had multiple bleeding and perforated ulcers in both stomach and duodenum, and the other had a bleeding ulcer on the anastomosis of a previous Billroth II gastrectomy. Both patients had comorbidity.

Table 2. Tariffs of frequently used interventions and hospitalization days, in Euro (€) *.

Therapeutic interventions	Tariffs
Suture repair: perforation (stomach)	782
Suture of bleeding vessel (duodenum)	792
Suture repair: perforation (duodenum)	1144
Endoscopic sclerosis of bleeding vessel (stomach)	354
Hospitalization days	
Normal care	332
Special care	735
Intensive care	1139

* 1 Euro = US $1.14.

Under- or overestimation of the costs of treatment of ulcer complications may have occurred for several reasons. To determine the costs of hospitalization days we used the tariff claimed at the insurance company of the patient. We did not incorporate the costs of medication separately because they are included in the tariffs of hospital care, and represent only a small part of the total cost of treatment. In addition, we did not estimate the costs of subsequent outpatient care. These factors point to underestimation of total costs. On the other hand, the study setting was a university hospital. This setting usually attracts patients with more severe and complicated disease. Also, costs in a university hospital are higher than elsewhere. This may also have resulted in overestimation of total costs.

Table 3. Mean (SD) costs per type of complication and per type of ulcer, in 1000 Euro*.

Complication	Major Costs**			Total Costs by Ulcer Type***	
	Costs of Hospitalization Days	Costs of Interventions	Total Costs	Ulcus Ventriculi	Ulcus Duodeni
All patients, n = 53					
Bleeding, n = 34	9.2 (10.1)	2.6 (4.4)	11.9 (13.7)	9.6 (14.8)	13.0 (13.8)
Perforation, n = 15	13.7 (10.8)	5.3 (3.5)	19.2 (13.7)	21.5 (15.4)	13.1 (4.4)
Bleeding and perforation, n = 4	20.1 (16.3)	5.5 (3.4)	26.0 (19.6)	54.1	16.8 (9.7)
Without comorbidity, n = 39					
Bleeding, n = 24	5.1 (4.4)	1.3 (2.3)	6.4 (6.2)	4.9 (3.2)	7.1 (7.2)
Perforation, n = 12	10.2 (5.8)	4.2 (1.6)	14.6 (6.6)	15.3 (7.7)	13.1 (4.4)
Bleeding and perforation, n = 3	22.6 (19.0)	6.4 (3.6)	29.2 (22.6)	54.1	16.8 (9.7)
With comorbidity uncorrected, n = 14					
Bleeding, n = 10	19.1 (13.0)	6.0 (6.3)	25.2 (17.8)	28.6 (31.6)	26.6 (16.1)
Perforation, n = 3	27.7 (16.3)	10.1 (5.4)	38.0 (20.2)	38.0 (20.2)	NA
Bleeding and perforation, n = 1	12.7	2.9	16.1	NA	NA
With comorbidity corrected, n = 14					
Bleeding, n = 10	15.7 (11.1)	3.6 (2.7)	19.5 (13.0)	13.0 (9.6)	22.8 (13.9)
Perforation, n = 3	21.1 (20.2)	8.7 (3.9)	30.0 (22.4)	30.0 (22.4)	NA
Bleeding and perforation, n = 1	12.7	2.9	16.1	NA	NA

* 1 Euro = US $1.14 ** Minor (untabulated) costs include costs of laboratory tests. *** Two patients could not be unequivocally classified: one had multiple bleeding and perforated ulcers in both stomach and duodenum, and the other had a bleeding ulcer on the anastomosis of a previous Billroth II gastrectomy. Both patients had comorbidity.

Personal, non-commercial use only. The Journal of Rheumatology Copyright © 2004. All rights reserved.

Downloaded on April 24, 2024 from www.jrheum.org

In another Dutch study, Chevat, *et al*[8] assessed the cost of treating serious GI events requiring hospitalization associated with the use of NSAID in patients with osteoarthritis and rheumatoid arthritis. They concluded that from a payers' perspective the total costs ranged between € 1800 and € 6900. Included costs were similar, with the addition of medication and outpatient costs. Information on the use of medication was gathered from national databases. However, the use of resources was determined in interviews with physicians such as general practitioners, gastroenterologists, rheumatologists, surgeons, and hospital specialists, which may not be a reliable source. As our study is based on individual patient data, we believe that our estimation is more reliable and better describes daily clinical practice. As such, the estimate will be useful in determining the cost-effectiveness of strategies aimed at reducing the risk of complicated peptic ulcers in longterm NSAID users.

Cost studies are not directly comparable across countries. For the purpose of comparison, the purchase power parities (PPP) values published by the Organisation for Economic Cooperation and Development could be used. PPP are the rates of currency conversion that eliminate the differences in price levels between countries. In addition, the unit costs of interventions and hospitalization days could be used to compare across countries (Table 2). Studies concerning NSAID-gastropathy and costs in the United States have provided an estimate of the costs of hospitalization for serious GI complications[9-11]. The reported costs were US $10,000–$20,000. However, the authors did not report how costs were calculated and what cost prices or tariffs were used to estimate these costs. We used a bottom-up approach to estimate costs, and our publication includes information on costs of serious GI complications per type of ulcus (ulcus ventriculi vs ulcus duodeni, and bleeding vs perforation) and separately for ulcers with or without comorbidity. Therefore, we believe that our cost estimate provides additional information compared to the ARAMIS (Arthritis, Rheumatism, and Aging Medical Information System) data. That the results are comparable and support each other is important. Also, our results show that the wide range reported may depend upon differences between bleeding and perforation, the anatomic area of the complication, or presence of comorbid illness. It is the type of information that is important as one tries to understand the influence of these complications on the patient and the health care system. Future economic evaluation is needed to evaluate this influence.

The hospital treatment of ulcer complications is costly, especially in patients with comorbid conditions. With appropriate caution, the results of this study are generalizable to other settings with similar levels of care, allowing estimation of costs after price adjustment.

REFERENCES

1. Wallace AJ. NSAID gastroenteropathy: current therapy and diagnosis. Drugs of Today 1997;33:115-22.
2. Lanza FL. Gastrointestinal toxicity of newer NSAIDs. Am J Gastroenterol 1993;88:1318-23.
3. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. N Engl J Med 2000;343:1520-8.
4. Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA 2000;284:1247-55.
5. Wolfe MM, Lichtenstein DR, Singh G. Gastrointestinal toxicity of nonsteroidal antiinflammatory drugs. N Engl J Med 1999;340:1888-99.
6. Chung SC. Peptic ulcer bleeding. Am J Gastroenterol 2001;96:1-3.
7. Lee FY, Leung KL, Lai BS, Ng SS, Dexter S, Lau WY. Predicting mortality and morbidity of patients operated on for perforated peptic ulcers. Arch Surg 2001;136:90-4.
8. Chevat C, Pena BM, Al MJ, Rutten FF. Healthcare resource utilisation and costs of treating NSAID-associated gastrointestinal toxicity. A multinational perspective. Pharmacoeconomics 2001;19 Suppl 1:17-32.
9. Singh G. Recent considerations in nonsteroidal anti-inflammatory drug gastropathy. Am J Med 1998;105:31S-8S.
10. Singh G, Rosen RD. NSAID induced gastrointestinal complications: the ARAMIS perspective — 1997. Arthritis, Rheumatism, and Aging Medical Information System. J Rheumatol 1998;51 Suppl:8-16.
11. Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. J Rheumatol 1999;26 Suppl 56:18-24.

Personal, non-commercial use only. The Journal of Rheumatology Copyright © 2004. All rights reserved.

Downloaded on April 24, 2024 from www.jrheum.org