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Transcatheter arterial embolization for gastroduodenal ulcers bleeding

Transkateterinė arterinė embolizacija gydant skrandžio ir dvylikapirštės žarnos opas

Audrius Širvinskas [1], Edgaras Smolskas[1], Kipras Mikelis[2], Gintautas Brimas[1]

[1] *Republic Vilnius University Hospital, 29 Siltnamiu Str., LT-01430 Vilnius, Lithuania*
[2] *Faculty of Medicine, Vilnius University, 21 M. K. Ciurlionio Str., LT-03101 Vilnius, Lithuania*
El. paštas: edgaras.smolskas@gmail.com

[1] *Respublikinė Vilniaus universitetinė ligoninė, Šiltnamių g. 29, LT-01430 Vilnius, Lietuva*
[2] *Vilniaus universiteto Medicinos fakultetas, M. K. Čiurlionio g. 21, LT-03101 Vilnius, Lietuva*
E-mail: edgaras.smolskas@gmail.com

Background and objective

Transcatheter arterial embolization is an alternative to surgical management when dealing with recurrent bleeding from a peptic ulcer after a failed endoscopic treatment. The purpose of this study is to analize the effectiveness and outcomes of transcatheter arterial embolization and identify the factors that influenced morbidity and mortality rates.

Materials and methods

A retrospective single-center analysis was performed of 20 patients who underwent transcatheter arterial embolization for acute upper gastrointestinal bleeding from gastroduodenal ulcers from 2012 to 2015 at the Republic Vilnius University Hospital. We analyzed the association of early rebleeding and mortality with sex, age, number of units of blood components administered to the patients, length of hospital stay, time passed until embolization, therapeutic or prophylactic embolization.

Results

The embolization procedure had a technical success rate of a 100%. 14 (70%) were prophylactic embolizations and 6 (30%) were therapeutic embolizations. Three patients (15%) had an episode of rebleeding following embolization, 5 (25%) patients died. Patients that died received statistically significant larger number of blood components (p=0.04 for frozen plasma; p=0.01 for packed red blood cells) and patients that survived had a shorter hospital stay (p=0.05). No associations were observed between rebleeding and factors analyzed.

Conclusions

Transcatheter arterial embolization is a feasible method for the treatment of rebleeding in gastroduodenal ulcer after endoscopic treatment, resulting in high rates of technical and clinical success and low complication rates. Further prospective randomized trials are needed to obtain more evidence.

Key words: peptic ulcer, hemorrhage, transcatheter arterial embolization

Įvadas

Transkateterinė arterinė embolizacija yra chirurginio gydymo alternatyva. Ji taikoma esant pakartotiniam kraujavimui iš skrandžio ar dvylikapirštės žarnos opos po nepavykusio kraujo stabdymo endoskopijos metu. Mes nagrinėjome transkateterinės embolizacijos efektyvumą, gydymo baigtis ir rodiklius, galinčius turėti įtakos sergamumui bei mirtingumui.

Metodai

Atlikome retrospektyviąją analizę, į kurią įtraukėme 20 pacientų, kuriems nuo 2012 m. iki 2015 m. Respublikinėje Vilniaus universitetinėje ligoninėje buvo atlikta transkateterinė arterinė embolizacija dėl ūminio kraujavimo iš viršutinės virškinamojo trakto dalies. Ieškojome ryšio tarp pakartotinio kraujavimo bei mirštamumo ir pacientų lyties, amžiaus, perpiltų kraujo komponentų vienetų, hospitalizacijos trukmės, laiko iki embolizacijos, atliktos embolizacijos rūšies (profilaktinė ar terapinė).

Rezultatai

Embolizacijos techninis efektyvumas buvo 100 %. Keturiolikai pacientų (70 %) buvo atlikta profilaktinė ir 6 (30 %) – terapinė embolizacija. Trims (15 %) pacientams po embolizacijos pasikartojo kraujavimas. Penki (25 %) pacientai mirė. Pacientams, kurie vėliau mirė, buvo perpilta statistiškai reikšmingai daugiau kraujo komponentų vienetų (šviežiai šaldytos plazmos p=0,04; eritrocitų masės p=0,01), jų hospitalizacija buvo ilgesnė (p=0,05). Statistiškai reikšmingų veiksnių, galinčių turėti įtakos pakartotinio kraujavimo dažniui, neradome.

Išvados

Transkateterinė arterinė embolizacija yra tinkamas metodas po endoskopinio gydymo pasikartojusiam kraujavimui iš skrandžio ar dvylikapirštės žarnos opų gydyti. Nors šis būdas pasižymi dideliu techniniu ir klinikiniu efektyvumu ir mažu komplikacijų dažniu, tačiau reikalingi tolesni atsitiktinių imčių tyrimai šio gydymo būdo tinkamumui pagrįsti.

Reikšminiai žodžiai: peptinės opos, kraujavimas, transkateterinė arterinė embolizacija

Introduction

Peptic ulcer disease is a common condition with a yearly incidence of more than 5 cases per 1000 persons [1] and bleeding occurs in as many as 15% of them [2]. It remains a medical emergency problem worldwide – up to 59% of nonvariceal acute gastrointestinal bleeding is attributed to bleeding from a peptic ulcer [1, 2]. The hospitalization rate for peptic ulcer disease decreased 35% from 71.1/100,000 in 1998 population to 46/100,000 population in 2010. Despite the wide usage of H2 receptor antagonists, proton pump inhibitors and antibiotic eradication of *H. pylori*, peptic ulcer bleeding remains a major problem with high mortality rates among the elderly patients – 20-30 deaths per 100 000 patients over the age of 65 years [3–5]. The main risk factors for peptic ulcer bleeding are non-steroidal anti-inflammatory drugs usage and comorbidities such as hepatic, renal or malignant diseases [6–8]. The initial treatment of choice in case of peptic ulcer bleeding alongside pharmacotherapy is endoscopic hemostasis, which significantly decreases rebleeding rates and mortality [9]. Endoscopy helps confirming the diagnosis and provides initial hemostasis options – epinephrine injections alongside clips, glue, coagulation or sclerosant injection [9–11]. If the first endoscopy is not successful, repeat endoscopic treatment is recommended, according to NICE guidelines [12]. However recurrent bleeding occurs in 5-10% [13, 14]. In such cases surgery was traditionally the treatment of choice, however, if expertise is available, NICE guidelines also recommend arterial embolization as an alternative to surgical treatment [15]. In 1972 Rosch *et al*. presented selective transcatheter arterial embolization for upper gastrointestinal bleeding control and since then it has been used successfully as an alternative to surgery in selected groups of patients [16–18]. Controversy remains regarding the gastroduodenal ulcers bleeding treatment algorithm.

Our purpose was to analize the effectiveness and outcomes of transcatheter arterial embolization and identify the clinical and technical factors that influenced the outcome of transcatheter arterial embolization and quantify the impact of those variables on morbidity and mortality rates.

Materials and methods

We performed a retrospective analysis of 20 patients who underwent transcatheter arterial embolization for acute upper gastrointestinal bleeding from gastroduodenal ulcers from 2012 November to 2015 November at the Republic Vilnius University Hospital. All of the

patients after endoscopy and confirmation of diagnosis were classified according to Forrest classification and administered conservative treatment upon arrival – intravenous bolus injection of proton-pump inhibitor (80 mg Omeprazol) and 40mg Omeprazol intravenously three times per day for three days. Patients with coagulation disorders had their coagulopathy corrected.

All of the 20 patients had shown clinical signs of rebleeding after initial endoscopic treatment (blood from nasogastric tube, low blood pressure, increase in pulse, low hemoglobin count) despite initial conservative medical therapy and local endoscopic treatment with adrenaline (1:10 000) injections. All angiographic procedures were performed with standard percutaneous transfemoral catheterization. Selective angiography of the celiac trunk, gastroduodenal artery and superior mesenteric artery was obtained using a 5-Fr catheter. Embolization performed after visualization of Ultravist contrast extravasation at angiography was referred to as "therapeutic embolization". When visualization of contrast extravasation on angiography was not seen, "prophylactic embolization" was performed. Embolization was carried out by placing various types of vascular VortX coils and no embolic agents other than coils were used. If the bleeding ulcer was in the fundus or corpus of the stomach, then the left gastric artery (LGA) was selectively embolized. If the bleeding ulcer was in the stomach antrum or duodenum, the gastroduodenal artery (GDA) was selectively embolized on both sides of the bleeding site to prevent 'back-door' effect – repeated bleeding related with retrograde perfusion. Postembolization angiography was performed to confirm the effect of embolization in all of the patients.

Demographic variables, clinical findings, endoscopic treatment, transfusion requirements before and after transcatheter arterial embolization, length of hospital stay, and outcomes including recurrent bleeding, need for surgery after transcatheter arterial embolization, and in-hospital death were recorded.

We analyzed the association between early rebleeding and following factors: sex, age, number of units of blood components administered to the patients, length of hospital stay, time passed until embolization and whether the embolization performed was therapeutic or empirical. Analysis was also carried out between mortality following embolization and factors mentioned above. Pearson's chi-square test was used to test for association between categorical data and Independent-samples t-test for continuous variables. Data processing was done using SPSS 20.0 software.

Results

Transarterial embolization was performed to twenty patients, 14 (70%) male and 6 (30%) female. The mean age of the patients was 65.6 (±17.13) years, ranging from 30 to 93 years. There was a mean time of 3.11 (±1.99) days, ranging from 0.8 to 8 days, that passed since the first symptoms of bleeding began to the time that embolization was performed.

There was an average of 8.35 (±4.21) units of packed red blood cells administered to the patients prior to embolization procedure. The mean of packed red cells received in total during the period patient was hospitalized was 11.90 (±5.35) units. An average of 6.20 (±5.85) units of frozen plasma was received by patients during transfusion procedures. Summary of patients characteristics are shown in Table 1.

In 5 (25.0%) of the 20 patients the cause of hemorrhage was determined to be a bleeding gastric ulcer (two from fundus et corpus, three from antrum) and in 15 (75.0%) patients bleeding was originating from a duodenal ulcer. The data of ulcers location and Forrest classification is summarised in Table 2.

In 18 (90%) cases site of the embolization was the gastroduodenal artery. The left gastric artery was targeted in two (10%) cases.

The embolization procedure had a technical success rate of a 100%. Of the 20 embolizations performed 14 (70%) were prophylactic embolizations and 6 (30%) were therapeutic embolizations, when bleeding site was visualized before embolization using angiography. During the procedure there were no complications. There were no gastrointestinal tract ischaemic complications in 30 days period. Procedural outcomes are shown in Table 3.

The average hospital stay after the embolization procedure was 14.90 (±9.78) days. 17 patients had no rebleeding within 30 days. Three patients (15%) had an episode of repeated bleeding. All three of these patients had a prophylactic embolizations. Two of these cases

Table 1. Summary of patients characteristics

Parameter	Mean	±SD
Mean age (years)	65.6	±17.13
Transfusion requirement		
Mean units of packed red cells (total)	11.90	±5.35
Mean units of packed red cells before TAE	8.35	±4.21
Mean units of frozen plasma	6.20	±5.85
Mean time from bleeding to TAE (days)	3.11	±1.99
Mean days of hospitalization	14.9	±9.78

Table 2. Forrest classification of peptic ulcers at primary endoscopy

Grade	N (%)	Gastric ulcer (%)	Duodenal ulcer (%)
Forrest IA	3 (15%)	0 (0%)	3 (15%)
Forrest IB	5 (25%)	1 (5%)	4 (20%)
Forrest IIA	5 (25%)	1 (5%)	4 (20%)
Forrest IIB	5 (25%)	2 (10%)	3 (15%)
Forrest IIC	1 (5%)	0 (0%)	1 (5%)
Forrest III	1 (5%)	1 (5%)	0 (0%)
Total	20 (100%)	5 (25%)	15 (75%)

Table 3. Procedural outcomes

Outcome	N	(%)
Embolization	20	100.0%
Prophylactic embolization	14	70.0%
Therapeutic embolization	6	30.0%
Technical success	20	100.0%
Rebleeding	3	15.0%
Complications	0	0.0%

Table 4. Factors associated with mortality

Factor	Died (Mean ±SD)	Survived (Mean ±SD)	t-test value	P value
Hospital stay	22.6 ±17.47	12.33 ±3.77	2.24	0.05
Units of frozen plasma	11.80 ±9.41	4.33 ±2.47	2.92	0.04
Units of packed red blood cells	17.00±4.85	10.20±4.44	2.90	0.01

were treated surgically and one patient had a repeated endoscopic treatment. 5 (25%) of the 20 patients, died from the reasons not related with non-stopped bleeding: from acute respiratory failure (n=3) multiple organ failure (n=1), sepsis (n=1). All five patients had a prophylactic embolization. The mean age of patients that died was 58.6 years. One of these patients underwent a surgical procedure for bleeding control, 4 had more than one additional diseases.

There was no statistically significant association of repeated bleeding and patient sex, age, time passed until hospitalization, therapeutic or prophylactic em-

bolization or number of units of blood transfused. Statistically significant differences were found between mortality and total number of units of packet red cells and frozen plasma administered to patients during their hospital stay – patients that died received a larger number of blood components. There was also a difference between the length of hospital stay – patients that survived had a shorter hospital stay. We found differences between mortality in female and male, therapeutic and prophylactic embolization, but not statistically significant (p= 0.09).

Discussion

The modality of choice for diagnosis and treatment of acute bleeding originating from a peptic ulcer is endoscopy. It provides options to stop the bleeding and has been shown to decrease rebleeding rates and mortality when used alongside proton pump inhibitors [19, 20]. However in some cases endoscopy fails to provide adequate hemostasis. The rate of such rebleeding after initial endoscopy has not been significantly decreasing in the last years and remains 8–10% [21]. Salvage therapies such as surgery or more recently – transcatheter arterial embolization have been used to control severe bleeding that does not respond to endoscopy. For cases where bleeding persists after a successful initial endoscopy, repeat endoscopy is the recommended method [14]. A randomized control trial compared repeat endoscopic treatment with surgery and found that surgery group had more postoperative complications; however such factors as ulcer size or hemodynamic instability lead to an unsuccessful endoscopic hemostasis [13]. Several studies have compared angiographic embolization and surgery over the years [18, 22, 23]. Angiographic embolization was associated with reduced treatment-related complications (20–54% vs 37–68%), but recurrent bleeding (RR 2, 95% CI 1.3–2.9) was more often after embolization [21]. A recent systematic review found no differences in mortality when comparing both of these methods [24]. Because it is less invasive as surgery and has a lower complication rate, arterial embolization is often reserved for high surgical risk patients [18, 25].

The complications of embolization are groin hematomas or acute renal failure, both of which are observed with the same rate as in other endovascular interventions [26]. Among the specific complications are bowel ischemia (0–16%) and duodenal stenosis (0–25%), which are rare because of the rich collateral blood supply of the targeted region [27, 28]. Unintentional hepatic artery embolization can cause liver failure, however this is more common for patients with liver cirrhosis [29]. In our study no specific complications were detected in 30 days period.

During thirty days period following embolization, three (15%) of our patients had an episode of repeated bleeding. The rate of rebleeding is lower than that reported by Loffroy *et al.* in their review of embolization for non-variceal upper gastrointestinal bleeding (33%) or the rate reported in literature review of embolization for gastroduodenal ulcer treatment (25%) [28, 30]. Coagulation disorders, larger number of blood components transfused, a longer time from the beginning of shock to the procedure, previous surgery for bleeding, corticosteroid intake and multiple comorbidities are among the factors shown to have a negative effect on the bleeding rates following arterial embolization [28, 30, 31]. We did not find any statistically significant associations between the factors analyzed and rebleeding in our cohort which could be attributed to a small patient base or that our retrospective study design did not allow us to accurately check for specific comorbidities or coagulation disorders.

The thirty day mortality was 25% in our patients, which is the same as reported in review by Loffroy *et al.* (25%) [30]. Among the factors that are known to effect the outcome of embolization therapy are advanced age, concomitant illnesses such as hepatic, renal or malignant diseases or massive blood transfusions [8, 28]. The mean age of our patients was 65.6 years which does not differ from the mean age presented in a recent literature review by Loffroy *et al.* (65 years) [28]. Such advanced age of the patients may be explained by the fact that embolization is often reserved for older patients who would be at a high risk for surgery [18]. The mean time that passed between the onset of symptoms and embolization of 3.11 days was longer than that reported by Loffroy *et al.* in their experience (2.3 days), however this did not prove to be a factor associated with rebleeding or mortality rates in our study. An association was also observed between the need of transfusions and thirty

days mortality. Similar factor association of massive blood loss and mortality has been reported by Larson *et al.* in their 115 patient series on upper gastrointestinal bleeding outcomes [34].

We observed differences in the outcome whether the source of the bleeding was visualized during angiography prior to embolization and thirty days mortality rates – no patients died in the therapeutic embolization group and 35.7% mortality was seen in the prophylactic embolization group. The difference comparing mortality was not statistically significant however, most likely due to our small patient base of twenty patients. Several other series report no difference in outcome between patients in the prophylactic embolization group and patients who had the source of the bleeding visualized prior to embolization [29, 32]. One explanation may be the abundant collateral circulation which continues to supply blood to the bleeding site [28, 32]. The approach we took to avoid possible retrograde bleeding was to use the 'sandwich' technique on the gastroduodenal artery during embolization, which should prevent additional bleeding from the superior mesenteric artery circulation.

The technical success rate was 100% in our patients and the clinical success rate was 80%. Such results fit well in the success rates published by other authors (91–100% technical success rate and 63–100% clinical success rate) [17, 32]. The high rates of both technical and clinical success and many studies confirming the results of the feasibility of arterial embolization as a method for treatment of endoscopically unmanageable peptic ulcer bleeding has led to accepting embolization as the salvage treatment of choice after a failed embolization. Furthermore, a recent studies have shown significant results while examining the role of transcatheter arterial embolization for prophylactic treatment of peptic ulcer bleeding after a successful endoscopy managed to stop the bleeding [35]. In patients with a high risk of rebleeding, this method reduced the rates of repeated bleeding episodes and the need for emergency surgery. Further studies on this approach are awaited to compare it with surgical treatment and endoscopic alternatives.

To conclude, transcatheter arterial embolization is a feasible method for the treatment of endoscopically unmanageable peptic ulcer bleeding, resulting in high rates of technical and clinical success and low complication rate. Further randomized prospective trials are needed to obtain more evidence and information.

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