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Research article

Endoscopic Variceal Ligation Outperforms Injection Sclerotherapy in Controlling Actively Bleeding Oesophageal Varices in Decompensated Cirrhotic Patients: A Real World Comparative Cohort Analysis

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Abstract

Background and aims: Although endoscopic variceal ligation (EVL) and injection sclerotherapy (IST) are both used to control acute bleeding, no detailed comparative data exist on the relative efficacy and outcome of each method in patients with actively bleeding ("spurting") oesophageal varices. This study compared the efficacy, safety and outcome of EVL with IST in controlling actively bleeding oesophageal varices. Methods: Forty cirrhotic patients with actively bleeding oesophageal varices (BOV) who received EVL were matched and compared with 40 who had IST. Control of variceal bleeding, rebleeding, variceal recurrence, endoscopic complications, eradication and survival were recorded using Baveno assessment criteria. Results: Primary endoscopic failure to control acute bleeding during the first endoscopic intervention occurred in 2.5% in the EVL group and 10% in the IST group. Secondary 5-day failure of bleeding control was 20% in the EVL group and 25% in the IST group. Overall successful endoscopic variceal bleeding during the index admission was similar (EVL 82.5% vs IST 72.5%). Endoscopic-related complications and bleeding from treatment-induced oesophageal ulceration was less common in EVL than in IST (5% vs 20%). Oesophageal variceal eradication was similar (EVL 82.4%, IST 87.5%). Survival outcome was similar (EVL 52.5%, range: 1-8 years; IST 50%, range: 3 months-12 years). Conclusion:EVL performed better than IST in achieving initial primary acute variceal bleeding control with similar secondary bleeding control at 5 days, with lower rebleeding rates and fewer procedure-related complications, but had no influence on 6 week or ultimate survival.

Keywords: oesophageal variceal bleeding, endoscopic variceal ligation, endoscopic injection sclerotherapy, rebleeding; variceal eradication, survival

Introduction

Acute variceal bleeding (AVB) is a severe and potentially life-threatening complication in patients with cirrhosis and portal hypertension with mortality rates as high as 20% for the index bleeding event and 10% for subsequent bleeding episodes [1-3]. Endoscopic intervention is the first-line treatment to control active bleeding, but around 60% of patients will rebleed after successful initial control if effective follow-up treatment is not provided [4]. Secondary prophylaxis to prevent further variceal bleeding is thus crucial and there is general consensus that patients surviving an initial bleeding episode should enter a long-term eradication and surveillance programme [4].

Endoscopic variceal ligation (EVL) has replaced injection sclerotherapy (IST) in most centres as the endoscopic treatment of choice, supported by data from randomised controlled trials (RCTs) which show more rapid eradication of varices with lower rates of rebleeding and fewer oesophageal complications with EVL [5]. However, detailed data on the relative success of each method in controlling AVB with actively bleeding ("spurting") varices are limited. The cohorts analyzed in previous RCTs comparing EVL with IST included only small numbers of patients with active variceal bleeding with conflicting results [5]. In the present study the comparative efficacies of EVL and IST in controlling actively bleeding oesophageal varices in patients in a high volume academic endoscopy referral centre are reported in the largest matched patient cohort to date.

Patients and Methods

Adult patients admitted to the Surgical Gastroenterology Unit in Groote Schuur Hospital, Cape Town with variceal bleeding between January 2000 and December 2018 were assessed. Only patients with actively bleeding ("spurting") oesophageal varices who received their first emergency and subsequent procedures in our unit were included in the study (Figure1). The outcome of endoscopic interventions, both emergency and sub-

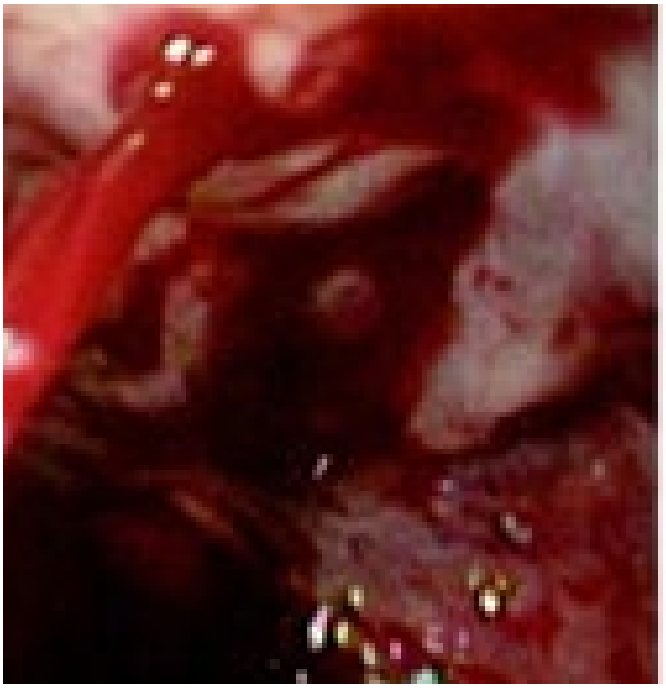

Figure 1. Actively bleeding "spurting" oesophageal varix

sequent elective, was analysed to assess the efficacy of EVL compared to IST in initial AVB control as well as long-term efficacy.

Study design

The study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for reporting observational studies [6]. A comparative case-matched analysis was done of consecutive patients who received their first emergency endoscopic intervention for actively bleeding ("spurting") oesophageal varices as well as subsequent procedures in our unit. Data were retrieved from a prospectively maintained faculty approved oesophageal varices registry and patients were manually matched one-to-one before outcome measures were reviewed [7]. To reduce bias, investigators were blinded throughout the selection and matching process to the primary and secondary end points [7]. The anonymized and de-identified data analysis included demographic and clinical information, cause of portal hypertension, Child–Pugh scores, haematology and liver function tests, liver biopsy, ultrasound and CT results, endoscopy information, variceal size, number of bands placed at each session, volume and frequency of sclerosant injections, number and interval of interventional sessions as well as procedure-related complications. Data entry for analysis was closed on 31 December 2019 to allow a minimum 12-month follow-up period. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Review Board of the Hospital and the University Ethics and Research Committee

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Study endpoints

The primary clinical endpoints of the study were: (i) primary endoscopic failure of the initial endoscopic intervention defined as failure to control AVB; (ii) secondary endoscopic failure defined as rebleeding within 5 days after initial endoscopic control; (iii) mortality during the initial hospital admission; (iv) 6-week mortality and (v) overall survival. The secondary endpoints were: (i) procedure-related complications and (ii) success in achieving variceal eradication as defined in the analysis criteria.

Acute bleeding management

Details of the acute bleeding management protocol in our unit have been published previously [8-10]. In brief, patients were managed with standard-of-care treatment according to an institutional protocol, which included intravenous fluid replacement, vasoactive drugs, antibiotics and endoscopic intervention. Resuscitation was commenced promptly, and transfusion initiated if the haemoglobin measured less than 8 g/dL. Octreotide was given as an initial IV bolus of 50 µg followed by a continuous infusion of 50 µg/hour for 72 hours and IV ceftriaxone 1 g/day as antibiotic prophylaxis. As soon as the patient was adequately resuscitated and stable, diagnostic endoscopy was performed to identify the source of bleeding. In patients in whom active bleeding could not be controlled a Sengstaken-Blakemore or Minnesota balloon tube was inserted for immediate tamponade and further endoscopic procedures were performed within 24 hours. When endoscopic measures failed TIPS was used as a rescue treatment.

Techniques of endoscopic intervention

A fibreoptic endoscope (model GIF 1T20 or K10, Olympus Corp., Lake Success, NY) was used during the first decade of the study and video-endoscopy in the latter decade. The techniques of both interventions as used in our unit have been described in detail previously [11-16]. For IST 5% ethanolamine oleate was injected using a combined intra- and paravariceal technique [12,13]. For large varices (grade 4 or 5) a maximum total volume of 25 ml sclerosant was injected at any one sclerotherapy session and generally smaller volumes when varices were grade 3 or less [10-12].

For EVL commercially available banding devices were used which included the Saeed Multi-band Ligator (Cook Endoscopy, Winston-Salem, North Carolina), and the Speedband Superview Super 7 Multiple Band Ligator (Boston Scientific Corp, Natick, Mass). During endoscopy for the sentinel bleed a band was applied first to incorporate the bleeding varix and then proximally in a helical fashion for approximately 10 cm to the remaining varices, regardless of size, starting at the gastro-oesophageal junction. A total of six bands was usually applied during the initial session, and progressively fewer bands at subsequent sessions as varices decreased in size. After the initial session during index admission, subsequent IST and EVL procedures were performed as an outpatient procedure at two-week intervals until the varices were eradicated. For patients treated with IST, eradication was defined as the absence of varices and for EVL as disappearance of varices or residual varices too small to be sucked and trapped in the banding device. After variceal eradication, surveillance endoscopy was performed at 3 and 6 months and then annually to identify patients in whom varices had recurred. All patients were given β–blockers during follow-up unless specifically contra-indicated.

Rebleeding

Baveno criteria were used to define secondary endoscopic 5-day failure to control bleeding [17,18]. Any recurrent bleeding episode after the first variceal ligation session or subsequently between scheduled treatment sessions was investigated by emergency endoscopy and treated according to endoscopic findings. Additional variceal ligation was undertaken if bleeding was due to residual or recurrent varices.

Statistical analysis

Student's t test was used to compare differences between groups for continuous variables, and the chi-square test was employed for categorical data. Kaplan–Meier survival curves were constructed and compared using the log-rank test. A p-value < 0.05 was considered significant. SAS System Package version 9.2.1 software (SAS Systems International, Cary, North Carolina, USA) was used for statistical analysis. Data were censored at the time of the last clinic visit or endoscopy session, TIPS placement or death.

Results

Demographic data, cause of cirrhosis, Child-Pugh grade and hepatic reserve of both groups were similar (Table 1). Overall endoscopic control of active bleeding was successful in 75 of the 80 patients (Table 2). In the two groups bleeding control during the index endoscopic procedure was achieved after EVL in 39 of 40 patients (97.5%) and in 36 of 40 patients (90%) after IST (Table 2). In the five patients, one in the EVL group and four in the IST group in whom active bleeding could initially not be controlled due to torrential bleeding, a balloon tube was used. All five were Child-Pugh grade C and 4 of the 5 (EVL n=1, IST n=3) ultimately died of liver failure aggravated by major blood loss despite eventual control of bleeding during the index admission.

Overall 18 (22.5%) of the 80 patients rebled during the index admission, all within 120 hours of the index endoscopy, and required 22 additional endoscopic procedures to control bleeding (Table 2). Five day failure of bleeding control was 20% in the EVL group and 25% in the IST group. Rebleeding from oesophageal varices during the index admission in the 2 groups was similar (EVL n=6 vs IST n=7). Overall eight patients (20%) in the EVL group rebled in hospital (varices=6, oesophageal ulceration=2) while ten patients (25%) in the IST group rebled in hospital (varices=7, oesophageal ulceration=3). Overall successful endoscopic control of variceal bleeding during the index admission was similar (EVL 82.5% vs IST 72.5%).

Overall more complications occurred in the IST group (20%) compared to the EVL group (5%) (p=0.08). Endoscopy-induced oesophageal ulceration was less common in EVL than in IST (3 vs 9). In the EVL group complications included encephalopathy (n=1) and drip phlebitis (n=1) while in the IST group complications included encephalopathy (n=1) and SBP (n=1).

Oesophageal varices were eradicated after EVL in 14 of the 17 patients (82.4%) who survived longer than 3 months after a median of 3 banding procedures (range 2 to 8), during a median of 6 months, (range 2 to 11 months) (Table 2). Oesophageal varices were eradicated after IST in 14 of the 16 patients (87.5%) who survived longer than 3 months after a median of 4 sclerotherapy procedures (range: 3 to 6) during a median of 7 months, (range: 3 to 10 months) (Table 2).

The overall index in-hospital admission mortality for both cohorts was 28.7% (n=23) with no significant difference in mortality rates (EVL n=13, IST n=10) between the two groups during the index admission (Figure 2). The 13 deaths in the EVL group were due to multi-organ and liver failure, five of which were precipitated by rebleeding; mortality in Child-Pugh group A was 0%, Child-Pugh B 15% and Child-Pugh C 52%. The 10 deaths in the IST group were due to liver and renal failure, five of which were aggravated by rebleeding; mortality in Child-Pugh group A was 0%, Child-Pugh B 5% and Child-Pugh C 50% (Table 2).

Median follow-up was 43.2 months (range 9-240 months). Six patients in the EVL group died of liver failure (n=4) or advanced HCC (n=2) at a median of 26 months, range: 1 month-6 years, none with further variceal bleeding. Ten patients in the IST group died of liver failure (n=4), advanced HCC (n=3), lung cancer (n=1) or due to variceal rebleeding (n=2) at a median of 26 months, range: 1 month-9 years (Figure 2). Overall mortality in the EVL group was 19 (47.5%) which included Child-Pugh group A 17%, Child-Pugh B 31% and Child-Pugh C 66.7%.

Table 1. Demographic, clinical, and endoscopic data in the IST and EVL cohorts

	Total n=80	IST n=40	EVL n=40
Male	56	28 (70%)	28 (70%)
Female	24	12 (30%)	12 (30%)
Age in years (range)	51 (r 22-86)	51 (r 25-86)	51 (r 22-82)
Cirrhosis - alcohol	56 (70%)	29 (72.5%)	27 (67.5%)
Cirrhosis - cryptogenic	8 (10%)	4 (10%)	4 (10%)
Cirrhosis - hepatitis B	5 (6.3%)	2 (5%)	3 (7.5%)
Cirrhosis - hepatitis B + alcohol	8 (10%)	4 (10%)	4 (10%)
Cirrhosis - NAFLD	2 (2.5%)	1 (2.5%)	1 (2.5%)
Cirrhosis - hepatitis C	1 (1.3%)	0	1 (2.5%)
Child-Pugh grade A	9 (11.3%)	3 (7.5%)	6 (15%)
Child-Pugh grade B	32 (40%)	19 (47.5%)	13 (32.5%)
Child-Pugh grade C	39 (48.8%)	18 (45%)	21 (52.5%)

IST: injection sclerotherapy, EVL: endoscopic variceal ligation

Table 2. Outcome: index admission, at 6 weeks, and overall survival in IST and EVL cohorts

	Total n=80	IST n=40	EVL n=40
Uncontrolled variceal bleeding despite endoscopic intervention	5 (6.3%)	4 (10%)	1 (2.5%)
Rebleeding after initial control	18 (22.5%)	10 (25%)	8 (20%)
(i) due to varices	13	7	6
(ii) due to ulceration	5	3	2
Blood transfusion (number of patients)	65 (81.3%)	31 (77.5%)	34 (85%)
Blood units transfused	6 (r 2-14)	4 (r 2-10)	6 (r 2-14)
Varices eradicated	27/33 (82%)	14/16 (88%)	14/17 (82%)
Index admission deaths	23 (28.8%)	10 (25%)	13 (32.5%)
Child-Pugh grade A	0/9 (0%)	0/3 (0%)	0/6 (0%)
Child-Pugh grade B	4/32 (12.5%)	2/19 (11%)	2/13 (15%)
Child-Pugh grade C	19/39 (49%)	8/18 (44%)	11/21 (52%)
Surviving patients: number of days in hospital	6 (range 1-31)	7 (range 1-31)	5 (range 1-14)
Index admission deaths (days alive)	1 (range 1-37)	1 (range 1-37)	2 (range 1-16)
6 week mortality	26 (32.5%)	12 (30%)	14 (35%)
Child-Pugh grade A	0/9 (0%)	0/3 (0%)	0/6 (0%)
Child-Pugh grade B	5/32 (16%)	3/19 (16%)	2/13 (15%)
Child-Pugh grade C	21/39 (54%)	9/18 (50%)	12/21 (58%)
Overall mortality	39 (49%)	20 (50%)	19 (48%)
Child-Pugh grade A	1/9 (11%)	0/3 (0%)	1/6 (17%)
Child-Pugh grade B	12/32 (38%)	8/19 (50%)	4/13 (31%)
Child-Pugh grade C	26/39 (67%)	12/18 (67%)	14/21 (67%)

IST injection sclerotherapy. EVL endoscopic variceal ligation

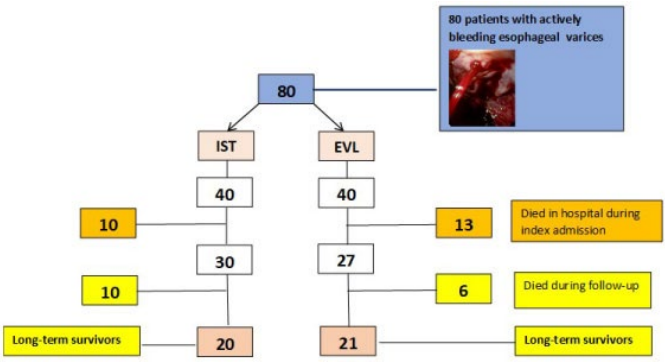

Figure 2. Outcome in the matched IST AND EVL patient cohorts
IST injections scierotherapy, EVL endoscopic variceal ligation

Overall mortality in the IST group was 20 (50%) which included Child-Pugh group A 0%, Child-Pugh B 42% and Child-Pugh C 66.7%. Forty-one of the 80 patients in the study are alive at a median of 3.6 years (EVL n=21, range: 1-8 years; IST n=20, range: 3 months-12 years).

Discussion

The principal objectives of endoscopic variceal intervention are expeditious control of acute bleeding and safe and cost-effective eradication of residual varices to prevent rebleeding. However, despite applying optimal standards of care, up to 10% of patients have persistent or recalcitrant variceal bleeding and 15% to 20% die during the first 6 weeks, often due to progressive liver or multi-organ failure aggravated by recurrent bleeding [4]. This matched observational comparative study in prospectively documented patients evaluated the best endoscopic method of controlling actively bleeding oesophageal varices at the index presentation. The study showed that EVL performed better than IST in controlling active bleeding during the first endoscopic intervention in patients with AVB and provided better bleeding control at 5 days with lower variceal rebleeding rates and less procedure-related complications, but ultimately had similar 6 week and overall survival rates compared to IST. While the superiority of EVL over IST did not achieve statistical significance, a numerical advantage was present in four of the five categories assessed with only recurrence of varices being worse. This study specifically used 5-day treatment failure and 6 week mortality as key bleeding outcomes as defined by Baveno criteria [17,18]. Both these specific time intervals are acknowledged as important primary endpoints and surrogate markers to provide global assessment of outcome of intervention in AVB and to establish international criteria and standards for interventional variceal endoscopic benchmarking [2,3,19].

No randomized study exists which specifically compares EVL with IST in patients who all had actively bleeding oesophageal varices encountered during the index endoscopy. In published trials and meta-analyses comparing EVL with IST only a minority of patients recruited had active bleeding so the compar-

Table 3. Summary of published randomized controlled trials of EVL vs IST

Author	Year	Number of patients	Number in each group		Control of bleeding		Varices eradicated		Eradication sessions		Rebleeding		Major complications		Variceal recurrence		Survival	
			EVL	IST	EVL	IST	EVL	IST	EVL	IST	EVL	IST	EVL	IST	EVL	IST	EVL	IST
Stiegmann 31	1992	129	64	65	86%	77%	55%	56%	4	5	36%	48%	**2%**	**22%**	33%	50%	**72%**	**55%**
Laine 32	1993	77	38	39	89%	89%	59%	69%	**4.1**	**6.2**	24%	31%	**24%**	**56%**	-	-	89%	85%
Gimson 33	1993	103	54	49	91%	92%	82%	71%	**3.4**	**4.9**	**30%**	**53%**	69%	65%	-	-	52%	18%
Lo 34	1995	120	61	59	94%	80%	74%	63%	**3.8**	**6.5**	**11%**	**36%**	**3.3%**	**19%**	-	-	**84%**	**68%**
Hou 35	1995	134	67	67	100%	88%	87%	79%	**3.5**	**4.6**	18%	33%	**4%**	**22%**	48%	30%	79%	84%
Sarin 36	1997	95	47	48	86%	80%	94%	94%	**4.1**	**5.2**	6.4%	20.8%	45%	50%	**28.7%**	**7.5%**	93%	89%
Baroncini 37	1997	111	57	54	-	-	93%	93%	**3.5**	**4.0**	16%	19%	**11%**	**31%**	**30%**	**13%**	79%	78%
Avgerinos 38	1997	77	37	40	-	-	95%	98%	**3.7**	**5.8**	27%	48%	**35%**	**60%**	31%	44%	80%	79%
Lo 20	1997	71	37	34	**97%**	**76%**	-	-	-	-	**17%**	**33%**	**5%**	**29%**	-	-	81%	65%
Siqueira 26	1998	40	20	20	-	-	90%	100%	3.1	3.7	0%	5%	-	-	0%	0%	100%	95%
De la Pena 39	1999	88	42	46	-	-	79%	71%	**5.3**	**6.6**	31%	50%	**14%**	**41%**	**47%**	**23%**	81%	78%
Masci 40	1999	100	50	50	-	-	88%	82%	**3.4**	**5.3**	**12%**	**42%**	**18%**	**38%**	32%	27%	80%	78%
Fakhry 27	2000	84	43	41	94%	94%	-	-	**2.8**	**4.8**	16%	15%	**2%**	**65%**	21%	20%	93%	93%
Zargar 41	2005	73	37	36	100%	83%	95%	92%	**3.7**	**7.7**	3%	19%	**3%**	**22%**	11%	9%	-	-
Villanueva 25	2006	179	90	89	**96%**	**85%**	-	-	-	-	7%	12%	**4%**	**13%**	-	-	87%	79%
Luz 42	2011	100	50	50	92%	96%	-	-	-	-	22%	14%	-	-	-	-	77%	80%
Ali 43	2017	124	60	64	100%	100%	87%	80%	-	-	23%	28%	**10%**	**27%**	-	-	78%	72%

EVL: endoscopic variceal ligation, IST: injection sclerotherapy, Bold highlighted comparisons are significant p<0.05

ative efficacy of either endoscopic method has never fully been tested or subjected to rigorous scientific scrutiny in this specific situation. This is the first study to critically evaluate the relative efficacies of EVL and IST in two comparative cohorts of patients all of whom had active oesophageal variceal bleeding at the time of the first endoscopy. In the only other similar comparative study from Taiwan, 71 cirrhotic patients who had either oozing or spurting variceal bleeding were randomized to receive EVL (37 patients) or IST (34 patients). Primary success rate defined as bleeding control for 72 hours was 97% in the EVL group and 76% in the IST group (P=.009). The efficacy of ligation was similar to sclerotherapy in the control of oozing varices (100% vs. 89%, P=.23), whereas ligation was superior to sclerotherapy in the control of spurting varices (94% vs. 62%, P=.012) 20. The strength of the data in the Taiwanese study is diluted by the inclusion of oozing varices unlike our study which was designed to evaluate the comparative efficacies of EVL and IST exclusively in patients with actively bleeding or "spurting" varices.

Five meta-analyses have evaluated the relative efficacies of EVL and IST for the treatment of patients with bleeding oesophageal varices. The first meta-analysis by D'Amico et al. included three RCTs and 309 patients in which pooled odds ratios (POR, 0.49; CI 0.31-0.78) showed a significant benefit from EVL [21]. Subsequently a second meta-analysis by Laine included seven randomized trials which showed that ligation reduced rebleeding (OR, 0.52 [95% CI, 0.37 to 0.74]), mortality (OR, 0.67 [CI, 0.46 to 0.98]), and death due to bleeding (OR, 0.49 [CI, 0.24 to 0.996]) compared with sclerotherapy [22]. The third meta-analysis assessed 12 trials involving 1309 patients. Seven of the trials included only patients with cirrhosis and a ligating device with an overtube was used in eight trials. The haemostatic efficacy of sclerotherapy was a median of 95% (76%-100%) compared with a median of 97% (86%-100%) for endoscopic ligation (p=0.4) with a 2.5% difference favoring ligation (95% CI 0.4% to 4.6%) (P=0.018). The mortality percentage difference was 1.3%, favoring ligation (95% CI-2.3% to 4.9%) (p = 0.46) [23]. A later fourth meta-analysis which included 13 trials and 1,091 patients showed that the risk of variceal rebleeding was significantly reduced by EVL (POR 0.46, 95% CI 0.35-0.60) and while there were no differences in mortality, complications were significantly less frequent and less severe with EVL and the number of endoscopic sessions needed to achieve eradication was significantly lower than with sclerotherapy [24]. The fifth and most recent meta-analysis by Dai et al. comprising 14 studies and 1236 patients showed EVL to be superior to IST with lower rebleeding and complication rates and a higher rate of variceal eradication [5]. In patients with actively bleeding varices undergoing EVL both rebleeding and variceal eradication were significantly lower (RR = 0.68, 95% CI: 0.57-0.81) and higher (RR = 1.06, 95% CI: 1.01–1.12) respectively in comparison to IST group [5]. The complication rate was significantly lower in EVL group compared to the IST group (RR = 0.28, 95% CI: 0.13-0.58) [5].

These published meta-analyses, however, have limitations which may influence the validity of the data and conclusions. Early studies included single band ligation devices which require repeated loading and passage through an oesophageal overtube, a cumbersome technique now outdated and replaced with modern multiband ligators. Sclerotherapy techniques in these studies were not standardised and varied widely in terms of sclerosant type, strength and volume used. In addition to variable needle size, the injection techniques also differed with either intravariceal, paravariceal or combined methods, as did the treatment intervals and schedules used [5]. Furthermore, included in the meta-analyses were studies from diverse countries with substantial differences in patient ethnicities, portal hypertension aetiologies, severity of hepatic decompensation and extent of oesophageal varices. The trials included in the meta-analyses also show conflicting results due to inconsistencies in design which included short patient follow-up of less than 6 weeks [25], heterogenous populations, some with a predominance of patients with schis-

tosomiasis, hepatitis B or C [26,27], or only extrahepatic portal vein occlusion or only children [28]. In one trial included in the meta-analysis more than half the patients had no history of variceal bleeding and received endoscopic intervention as primary prophylaxis [29] while in another trial included in the meta-analysis patients were randomized to either EVL or combined EVL and IST [30], factors which should have excluded the inclusion of these studies in the meta-analysis. In an accurate updated evaluation of the 17 randomized trials which compare EVL with IST (Table 3) EVL performed significantly better than IST in controlling bleeding (2 trials), with less rebleeding (5 trials), less endoscopy-related complications (13 trials), in fewer endoscopy sessions to achieve variceal eradication (11 trials) and improved survival (2 trials). However, varices recurred significantly more commonly after EVL than IST in 3 trials [31-44].

Experts agree that endoscopic control of variceal bleeding, especially during profuse bleeding, requires a high level of manipulative skill, experience and mature judgement. Despite initial scepticism and concerns that EVL would prove less effective than sclerotherapy in achieving control of actively bleeding varices, EVL was superior to IST in arresting "spurting" varices in this study and there were very few failures of acute haemostasis. These findings are contradictory to the general belief in which some authorities claim that EVL may be more difficult to perform than IST during active variceal haemorrhage because the reduced field of view and the visual constraints imposed by blood or clot filling the cap during profuse bleeding may obscure vision and limit accurate deployment of bands [34]. In addition, as banding has evolved, advances in equipment design and, in particular, the advent of multiband ligating devices have provided better compliance and lessened the discomfort of EVL [34].

Endoscopic failure to control variceal bleeding is encountered by even the most experienced endoscopists [45]. Up to 20% of VH episodes can be refractory to standard therapy and are associated with increased mortality [4]. This study emphasizes the critical importance of initial control of variceal bleeding during the first endoscopic intervention when active bleeding is present [44-46]. While neither method of endoscopic intervention has any effect on portal flow or resistance, the mechanisms of action differ. EVL utilizes mechanical strangulation in which the dimensions and design of the banding device limit the volume of the ligated tissue with less collateral oesophageal wall damage and less local complications. In contrast, IST produces a chemical thrombosis after needle puncture and injection of sclerosant into or adjacent to the varix with substantially higher local oesophageal complication rates [47]. Overall, our study demonstrated more complications in the IST group compared to the EVL group, findings similar to previous studies that demonstrate fewer side effects after ligation compared to sclerotherapy [5]. The major drawback of EVL is a higher tendency to variceal recurrence. Accumulated evidence suggests that patency of variceal para-oesophageal and peri-oesophageal feeder vessels predisposes to variceal recurrence. These feeder vessels are occluded more efficiently by sclerotherapy than ligation, which is usually confined to the mucosal and submucosal collaterals. Furthermore, the recurrence of varices may become more frequent with time [48].

Our study has several limitations. First, the study was conducted in a single-centre academic tertiary referral centre with experienced on-call endoscopists and staff available around the clock, thus patient selection and treatment bias may occur as similar advanced interventions may not be available or replicated in smaller hospitals. Second, the number of patients with failure was small and insufficient to identify criteria influencing endoscopic failure. The use of "all-cause rebleeding" was applied as a strategy to minimize bias in the definition of rebleeding. Even with these limitations, this study provided robust data that corroborates previous evidence.

In conclusion, this single centre comparative matched study showed that EVL outperformed IST with higher efficacy and lower complication rates and provides further confirmation, in particular, of the safety of EVL. EVL is established as the optimal endoscopic method for controlling active variceal bleeding and the long-term eradication treatment of oesophageal varices despite the higher tendency to recurrence. Recurrences did not impose a higher risk of rebleeding or require more sessions for further eradication if patients underwent regular endoscopic surveillance. The essential future requirements for improving survival in these high-risk patients are self-evident and include effective control of AVB, prevention of further rebleeding and minimising deterioration of liver function.

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