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Clinics and Research in Hepatology and Gastroenterology

EXPERIENCE WITH THE USE OF A HEMOSTATIC POWDER IN 152 PATIENTS UNDERGOING URGENT ENDOSCOPY FOR GASTROINTESTINAL BLEEDING

--Manuscript Draft--

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Abstract:	<p>Background and Study Aims</p> <p>In the recent years, topical hemostatic powders have been used for the management of upper gastrointestinal bleeding. The aim of this study was to report on the use of an hemostatic powder (Hemospray®), outside regular hours, by on-call endoscopists during urgent endoscopic procedures.</p> <p>Material and methods</p> <p>In this retrospective multicenter cohort study, consecutive patients having undergone an urgent endoscopy with the use of Hemospray® from November 2015 to December 2018 in the Paris and suburbs area were included. We collected clinical, biological and endoscopic variables. The outcomes such as the recurrence, repeat endoscopy and hemostatic treatment need, complications and survival were also collected.</p> <p>Results</p> <p>A total of 152 patients (mean 65 years old, 70.4% male) were included. Amongst the 31 endoscopists, 11 were "more experienced", and performed 48% of the endoscopies. The most common causes of bleeding were peptic ulcer (47.7%), malignancy (22.2%) and esophagitis (12.4%). Most bleedings originated from the upper GI tract (95.0%). Hemospray® was used as a salvage therapy in 60.8% of cases. Other hemostatic techniques were used in 52.9% of cases. Immediate bleeding cessation was noted in 79.0% of cases, recurrence in 39.9% of cases, and 26.4% of patients benefited from a repeat endoscopic hemostasis. 34 (23.0%) patients required a non-endoscopic treatment. At day 30, the survival rate was 71.6%. One complication</p>

	<p>was reported (perforation).</p> <p>Conclusions</p> <p>Hemostatic powder application by on-call endoscopists outside regular hours is technically feasible, but comes with a high risk of rebleeding in severely ill patients.</p>
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4 **EXPERIENCE WITH THE USE OF A HEMOSTATIC POWDER IN 152**
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6 **PATIENTS UNDERGOING URGENT ENDOSCOPY FOR**
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8 **GASTROINTESTINAL BLEEDING**
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15 Anne Guillaumot⁵, Einas Abou Ali⁵, Maximilien Barret⁵, Aurélien Amiot⁶, Nicolas Carbonell¹,
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Specific author contributions: AB, CH, MC: Conception and study design, data collection and analysis, drafting and revising of the manuscript. MLTM, NS, DD, MAG, EAA, MB, AA, NC, PM, UC, XD: analysis, drafting and revising of the manuscript.

Conflicts of interest:

Dr Marine Camus is a consultant for Boston Scientific and Cook Medical.

Dr Xavier Dray has acted as a consultant for Alfasigma, Bouchara Recordati, Boston Scientific, Fujifilm, Medtronic, and Pentax. Author Xavier Dray is also cofounder and shareholder of company Augmented Endoscopy.

Dr Maximilien Barret is a consultant for Norgine and Medtronic.

Drs Aymeric Becq, Charles Houdeville, My-Linh Tran Minh, Nils Steuer, David Danan, Marie Anne Guillaumot, Einas Abou Ali, Aurélien Amiot, Nicolas Carbonell, Philippe Marteau and Ulriikka Chaput have no conflicts of interest or financial ties to disclose.

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4 **ABSTRACT**
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7 *Background and Study Aims*
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9 In the recent years, topical hemostatic powders have been used for the management of upper
10 gastrointestinal bleeding. The aim of this study was to report on the use of an hemostatic powder
11 (Hemospray®), outside regular hours, by on-call endoscopists during urgent endoscopic
12 procedures.
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16 *Material and methods*
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18 In this retrospective multicenter cohort study, consecutive patients having undergone an urgent
19 endoscopy with the use of Hemospray® from November 2015 to December 2018 in the Paris and
20 suburbs area were included. We collected clinical, biological and endoscopic variables. The
21 outcomes such as the recurrence, repeat endoscopy and hemostatic treatment need, complications
22 and survival were also collected.
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27 *Results*
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29 A total of 152 patients (mean 65 years old, 70.4% male) were included. Amongst the 31
30 endoscopists, 11 were “more experienced”, and performed 48% of the endoscopies. The most
31 common causes of bleeding were peptic ulcer (47.7%), malignancy (22.2%) and esophagitis
32 (12.4%). Most bleedings originated from the upper GI tract (95.0%). Hemospray® was used as a
33 salvage therapy in 60.8% of cases. Other hemostatic techniques were used in 52.9% of cases.
34 Immediate bleeding cessation was noted in 79.0% of cases, recurrence in 39.9% of cases, and
35 26.4% of patients benefited from a repeat endoscopic hemostasis. 34 (23.0%) patients required a
36 non-endoscopic treatment. At day 30, the survival rate was 71.6%. One complication was reported
37 (perforation).
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45 *Conclusions*
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47 Hemostatic powder application by on-call endoscopists outside regular hours is technically
48 feasible, but comes with a high risk of rebleeding in severely ill patients.
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54 **Keywords:** Hemospray®, hemostatic powder, digestive bleeding, gastrointestinal hemorrhage
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ABBREVIATIONS

- GIB: Gastrointestinal bleeding
- UGIB: Upper gastrointestinal bleeding
- PUD: Peptic ulcer disease
- POET: Parisian On-call Endoscopy Team

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4 **INTRODUCTION**
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7 Acute gastrointestinal bleeding (GIB) is a common condition, associated with a significant
8 morbidity and mortality (1,2). Mortality rates have been reported ranging from 3 to 14%,
9 depending on the age, co-morbidities, clinical status, cause of bleeding (1,2). Upper
10 gastrointestinal bleeding (UGIB) accounts for over 80% of all GIB. Guidelines on the management
11 of variceal and non-variceal UGIB have been published (3,4). Endoscopic hemostasis is the
12 cornerstone of the management of GIB and relies on injection, thermal and mechanical therapies
13 (5). Injection therapy (epinephrine, sclerosing agents, and glue), thermocoagulation (including
14 plasma argon coagulation and bipolar electrocautery), as well as hemostatic clips and band ligation
15 have been shown to be effective methods in this setting (6–9). However, they are not always
16 efficient and offer limited success in cases of large bleeding areas (i.e. malignancy) (10).
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27 In the more recent years, topical hemostatic powders such as Hemospray® (TC-325; Cook Medical,
28 Winston-Salem, NC, USA) have been tested on porcine models, then used for the management of
29 UGIB in humans (10–14). Hemospray® is an inorganic, absorbent powder, which upon contact
30 with the moisture of an active bleeding, becomes coherent, creating a mechanical barrier. It also
31 activates platelet aggregation and possibly concentrates coagulation factors (10). The resulting
32 coagulum typically sloughs off within 24 hours (15). Hemospray® has received clearance in
33 multiple countries, specifically in Europe and has recently been FDA approved (11,16). Only a
34 few number of studies have been published on Hemospray®, showing it to be technically feasible
35 and a viable option as primary or salvage hemostatic treatment of UGIB (17–19).
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44 The goal of our study was to report on the real-life use of Hemospray®, in the setting of urgent
45 endoscopies, performed by mobile on-call endoscopists, outside regular hours, in multiple Parisian
46 teaching hospitals.
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52 **PATIENTS AND METHODS**
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55 We performed a retrospective descriptive multicenter cohort study to investigate the use of
56 Hemospray® during emergencies, by on-call endoscopists. This study was approved by the local
57 ethics committee. IRB approval was not required for this study. Patients' data was de-identified.
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4 Outside regular hours (nights and week-ends), urgent endoscopy procedures are performed by an
5 on-call endoscopist in over 20 Parisian teaching hospitals, covering a 5 million inhabitant area. All
6 endoscopists are senior attending physicians, fully trained in all the hemostatic techniques. All
7 have received hands-on training sessions on the use of Hemospray[®]. A taxicab is used to go from
8 one hospital to another. The endoscopist is based at Saint-Antoine Hospital where all the
9 equipment is stored. The on call team and equipment is transported by taxicab to perform
10 hemostatic technics such as clipping, epinephrine injection, band ligation, thermocoagulation and
11 hemostatic powder application (**figure 1**).
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21 We included consecutive patients having undergone an urgent endoscopy with the use of
22 Hemospray[®] from November 2015 to December 2018. The indication and treatment decision
23 making was at the discretion of the endoscopist. Hemospray[®] was applied using the standard
24 seven-French catheter with its tip a few centimeters from the bleeding source. The endoscopist
25 was assisted by a nurse and performed bedside endoscopies in intensive care units with a portable
26 endoscopy processor (Tele Pack X GI, Karl Storz SE & Co. KG, Tuttlingen, Germany), non-
27 therapeutic gastroscopes (Karl Storz Silver Scope – 13821 PKSK/NKSK, Karl Storz SE & Co.
28 KG, Tuttlingen, Germany), and a portable electrosurgical unit (ERBE – VIO100C, Erbe
29 Elektromedizin GmbH, Tuebingen, Germany). The procedures were **all** performed with general
30 anesthesia, after patient intubation, **given the high risk of aspiration in UGIB secondary to blood-**
31 **filled esophagus and/or stomach, or because in these urgent settings patients are not always with**
32 **empty stomach as they may have recently eaten or drank**. Salvage therapy was defined as the
33 application of Hemospray[®] for persistent bleeding after failure of other hemostatic modalities
34 either during the same endoscopic procedure or after failure of previous endoscopic attempts.
35 Immediate hemostasis was defined as the absence of ongoing visible active bleeding after
36 Hemospray[®] application. Recurrence was defined as the requirement of a subsequent hemostatic
37 treatment, meaning either a repeat endoscopic treatment and/or a non-endoscopic treatment
38 (arterial embolization, surgery, radiation therapy) within 30 days.
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55 We collected clinical data. Data regarding the hemorrhagic event was also collected. History of
56 recent endoscopy in the 30 days prior to the one performed by the on-call endoscopist with use of
57 Hemospray[®], and hemostatic treatment requirement was collected. Endoscopic findings were
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4 collected as well: cause, origin, type of bleeding, other hemostatic techniques used, primary or
5 salvage Hemospray[®], number of kits used, technical issues, and immediate efficacy. Outcomes
6 were collected, including the need for repeat endoscopy at day 3 and 30, subsequent endoscopic
7 or non-endoscopic hemostatic treatment, complications, and survival at day 30. The level of
8 experience of the on-call endoscopist was collected. We considered an endoscopist as “less
9 experienced” if he had been participating in on call shifts for less than four years at the start date
10 of data collection (i.e. November 2015). We considered an endoscopist as “more experienced” if
11 he had been participating in on-call shifts for more than four years at the start date of data
12 collection.

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21 The primary outcome of the study was the rate of bleeding recurrence which was calculated based
22 on the number of subsequent hemostatic interventions needed. The secondary outcomes were the
23 technical feasibility, the use of Hemospray[®] as a primary treatment, and the survival at 30 days.

24 25 26 27 28 29 30 **RESULTS**

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32 In the span of the 3 years of the study period, 2840 endoscopies were performed during non-
33 working hours for suspected bleeding, with hemostatic treatment in 1143 of cases (40.2%).
34 Hemospray[®] was used in 13.4% of all procedures with hemostatic treatment, accounting for 11%
35 of endoscopies performed for hemostatic purposes in 2016, 8% in 2017 and 11% in 2018. During
36 the study period, 152 patients underwent 153 endoscopic procedures in the setting of acute GIB
37 with Hemospray[®] application. Four patients were excluded due to missing follow-up data (4) (**flow**
38 **chart**). These endoscopies were performed by 31 different endoscopists. Amongst these
39 endoscopists, 11 were ‘less experienced’ and performed 73 of the 153 endoscopies (48%).

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48 The mean age of the patients was 65.0 ± 12.2 years. 70.4% of patients were male and 61 patients
49 (40.1%) were on an antiplatelet and/or anticoagulant medication. Sixty-four patients (42.1%)
50 required a vasopressive drug and 142 (93.4%) blood transfusion (**table 1**).

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Forty-six (30.1%) had endoscopic procedures within the 30 days prior, 26 (56.5%) of which
received hemostatic treatment. The most common causes of bleeding were peptic ulcer disease
(PUD) (47.7%), bleeding tumors (22.2%) and esophagitis (12.4%). Amongst the nine patients with

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4 post-endoscopy bleeding, five were secondary to a sphincterotomy. One patient had an
5 aortoenteric fistula. Most bleedings were localized in the upper GI tract (95.0%) and were active
6 (95.4%). Regarding the four patients with non-active bleeding, two had a post-sphincterotomy
7 bleed with a clot seen at the level of the papilla. Hemospray[®] was used as a primary therapy in 60
8 cases (39.2%) and as a salvage therapy in 93 cases (60.8%). The use of Hemospray[®] as a primary
9 or salvage therapy was similar between “less” and “more” experienced endoscopists (38% and
10 40% as a primary therapy, and 62 and 60% as a salvage therapy, respectively) (**figure 2**). Other
11 hemostatic techniques were used in 81 cases (52.9%). Immediate bleeding cessation was noted in
12 121 cases (79.0%). Use of 2 Hemospray[®] kits was required in one patient (0.7%). Hemospray[®]
13 application was challenging in five cases (3.3%) (**table 2**). Among the patients with persistent
14 bleeding, 7 (43.7%) had received Hemospray[®] as a primary therapy and 9 (56.3%) as a salvage
15 therapy. Among the patients with bleeding, 41 (33.9%) had received Hemospray[®] as a primary
16 therapy and 80 (66.1%) as a salvage therapy (**figure 3**).

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30 Four patients were lost to follow-up. Seventy-one patients (48.0%) required 88 repeat endoscopic
31 procedures for suspected recurrence. A repeat endoscopy was required in 37 patients before day
32 3, in 17 patients before day 30, and in 17 patients before day 3 and a second time before day 30.
33 Thirty-nine patients (26.4%) required a repeat hemostatic treatment (48 endoscopies) (**table 3**).
34 Thirty-four (23.0%) patients required a non-endoscopic hemostatic treatment such as arterial
35 embolization (9.5%), surgery (8.8%), arterial embolization followed by surgery (2.7%) and
36 radiation therapy (2.0%). Overall, 59 (39.9%) patients had a recurrence requiring endoscopic
37 and/or non-endoscopic hemostatic treatment. Fourteen (9.5%) patients required both endoscopic
38 and non-endoscopic hemostatic treatment. One perforation was reported. Verification of the
39 patients’ records showed the diagnosis was made by Computed Tomography, 48 hours after the
40 endoscopy, because of worsening clinical condition. Based on the endoscopy report, the patient
41 had a deep peptic ulcer and there was no suspicion of perforation prior or during the endoscopy.
42 At day 30, 106 patients (71.6%) had survived (**table 3**). Finally, 23% and 33% of patients with and
43 without bleeding cessation respectively did not survive after 30 days of follow-up (Odds
44 Ratio 0.69, 95% Confidence interval [0.21; 2.63], Fisher’s exact test, p = 0.55) (**Figure 4**).
45 Immediate hemostasis was achieved in 121 (79%) patients, amongst which 40.9% (49 patients)
46 did not require further treatment (endoscopic or non-endoscopic) and survived at 30 days. Overall,
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4 57 (37.5%) of the 152 patients did not require further treatment (endoscopic or non-endoscopic)
5 and survived at 30 days, regardless of initial bleeding cessation.
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10 11 **DISCUSSION**

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13 In this study, we report on the real life use of the hemostatic powder Hemospray[®], in the setting
14 of urgent endoscopic procedures performed outside working hours, by mobile on-call
15 endoscopists. Hemospray[®] was mostly used for upper GIB (95.0%), nearly half of which were due
16 to PUD (47.7%). Hemospray[®] was used as salvage therapy in 60.8% of cases. During follow up,
17 39.9% had a recurrence. At 30 days of follow-up, the mortality rate was 28.4%.
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24 The use of Hemospray[®] by our group was stable after becoming available and did not increase
25 with the endoscopists experience. It's use accounts for 10% of all our cases. It should however be
26 noted that one third of our patients had a prior procedure, nearly two thirds benefited from
27 Hemospray[®] as a salvage therapy, and that these endoscopies were performed in an urgent setting,
28 in non-dedicated units.
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35 Our study adds to the existing body of literature regarding the use of Hemospray[®]. First, our study
36 serves to show that Hemospray[®] application is user friendly, consistent with previously published
37 data. The application was challenging in five cases (3.3%), due to difficult anatomy, scope position
38 and/or obstruction of the catheter. Second, previous studies have reported on the efficacy of
39 Hemospray[®] application in acute GIB (17–21). The largest study to this day, published in 2019 by
40 Alzoubaidi et al., included 314 patients. The immediate efficacy rate was 89.5%. The recurrence
41 rate amongst these patients was 10.3%. The 30-day all-cause mortality was 20.0% (63 of 314
42 patients) (20). A meta-analysis by Faccuirusso et al. including 1063 patients showed an immediate
43 hemostasis rate of 93.5%, a 30 day recurrence rate of 16.9%, and an all-cause mortality rate of
44 7.6% (22). In our study, the immediate efficacy rate was 79%, the recurrence rate was 39.9%, and
45 28.4% of patients did not survive at day 30. The plausible reasons for these differences are many.
46 In our study, 92% of patients had comorbidities, and 42.1% required vasopressive support. The
47 mean hemoglobin level was very low (7 g/dL), 93.4% were transfused, 40.1% were on an
48 antiplatelet and/or anticoagulant medication, and 17% had prior endoscopic hemostatic treatment
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4 in the last 30 days. Furthermore, endoscopies were performed in difficult conditions: non-
5 dedicated units, overnight or during weekends.
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8 A majority of our patients with bleeding cessation had Hemospray[®] as salvage therapy (66.1%).
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10 Amongst the 16 patients with ongoing bleeding, Hemospray[®] as primary or salvage therapy did
11 not seem to differ (7 of the 60 patients with Hemospray[®] as primary therapy vs. 9 of the 93 patients
12 with Hemospray[®] as salvage therapy). We do not believe, based on these results, that Hemospray[®]
13 should be specifically used as salvage therapy. In some cases, Hemospray[®] would naturally appear
14 as the first and only choice of treatment (i.e. extensive esophagitis, large tumors), and it seems the
15 rate of ongoing bleeding would not be higher. However, given the cost of this treatment, future
16 studies should specifically assess whether or not it is a cost-effective treatment or not, especially
17 given the likely lower efficiency as a primary therapy.
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20 There was no statistical difference between patients with or without bleeding cessation in terms of
21 mortality rate at day 30 (23 vs 33%, p-value: 0.55). This was unsurprising as severely ill patients
22 likely die of other causes, especially those with bleeding cessation, as shown in a previously
23 published study (22).
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26 Finally, after other hemostatic techniques had failed, or were judged inappropriate, Hemospray[®]
27 yielded an immediate bleeding cessation in 121 patients, 40.5% of which did not require further
28 intervention and had survived at 30 days of follow-up. Given the temporary hemostatic effect of
29 Hemospray[®], these results suggest that this technique can be a positive step in stopping an acute
30 bleeding. However, the rebleeding (41.3%, 50/121) and mortality (22.3%, 27/121) rates were
31 significant in these patients. We believe that when Hemospray[®] has been beneficial at first, close
32 monitoring should be implemented to avoid delay of further non-endoscopic hemostatic treatment
33 if needed.
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36 All in all, Hemospray is mostly used as salvage therapy in UGIB, when other techniques have
37 failed, but can also be used as a first line hemostatic treatment when appropriate. Hemospray
38 application should be considered as a temporary treatment, and as being a potential bridge to a
39 non-endoscopic treatment in some cases.
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55 Guidelines recommend the use of Hemospray[®] in active non-variceal upper GIB. In this study,
56 Hemospray[®] was mainly performed in patients with upper GIB (95.0%). In addition, it was used
57 on active bleeding in 95.4% of cases. Amongst the four patients with non-active bleeding, two had
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4 a post-sphincterotomy bleeding, difficult to treat given the lack of proper equipment available here.
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6 In the two other cases (gastric ulcerations with minor stigmata of recent hemorrhage), using
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8 Hemospray[®] was not appropriate. Studies have described the use of Hemospray[®] in various causes
9
10 of lower GIB, with high rates of immediate hemostasis (10,23,24). Interesting results have been
11
12 published in severe diverticular bleeding with immediate hemostasis in a series of ten patients,
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14 with no recurrence (24). In our experience, Hemospray[®] was used for lower GIB (malignancy,
15
16 varices, ulcer, ischemia) in nine patients. However, there is insufficient data to suggest its routine
17
18 use in this setting.
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21 In previously published studies, Hemospray[®] was mainly used in GIB secondary to peptic ulcers,
22
23 malignancies and post-endoscopy (11,19). Our study shows a different clinical practice. Although
24
25 Hemospray[®] was used first in PUD and second in malignancy cases, a significant portion of
26
27 applications were for esophagitis and post-endoscopy bleeding. In addition, it was used in five
28
29 patients for esophageal variceal bleeding. Several studies have reported on the use of Hemospray[®]
30
31 in variceal GIB. In a review dating from 2015, hemostasis was achieved in 100% of nine cases of
32
33 variceal GIB (10). A randomized controlled trial including 86 patients compared early hemostatic
34
35 powder application followed by early elective endoscopy to early elective endoscopy only. The
36
37 rate of rescue endoscopy was significantly lower in the hemostatic powder group (12% vs 30%,
38
39 p=0.034) (25) and the survival was higher (30% vs 7% p=0.006). Finally, in our cohort,
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41 Hemospray[®] was used once in a case of an eso-aortic fistula, which was not known at the time.
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44 Complications of Hemospray[®] are infrequent. We report one case of perforation. The likelihood
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46 of Hemospray[®] application being the cause of this perforation is difficult to establish but probably
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48 low. This is consistent with previously published data and concurs with the safe profile of
49
50 Hemospray[®]. In the study by Alzoubaidi et al., there were no complications (20). In the review by
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52 Chen et al. including 243 cases, 5 complications were reported (10): pain, splenic infarct (unclear
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54 if related), transient biliary obstruction (post sphincterotomy bleeding), and hemoperitoneum
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56 (unclear if related). In theory, there is a risk of vascular embolization, bowel perforation, and bowel
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58 obstruction. Embolization has however never been described. Caution is warranted in case of a
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60 thin wall at risk for perforation, and near the ampulla because of the risk of biliary obstruction.
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Several limitations of our study can be outlined. First, this study was retrospective. This was a multicenter study adding to the difficulty in collecting data retrospectively, specifically regarding follow-up. Second, no consensus regarding the criteria used for decision-making (procedure indication and per endoscopy treatment) was established prior to the study. However, this study reports real-life use of Hemospray[®] during non-working hours, in a setting where physicians do not always have much experience, where potential assistance (i.e. other physicians) is non-existent and where fatigue of the on-call endoscopist could play a significant role in the decision making process.

In conclusion, Hemospray[®] application by on-call endoscopists outside regular hours is technically feasible, primarily used for UGIB, mostly secondary to peptic ulcers and malignancy related bleeding, and mainly as a salvage therapy. Its use carries a very low risk of complication. Although recurrence and mortality rates appear to be higher as compared to previously published studies, 40.5% of our patients did not require a further intervention and were alive at day 30 of follow-up, despite being severely ill.

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FIGURE LEGENDS

Figure 1: Endoscopic portable equipment

Figure 2: Use of Hemospray depending on endoscopist experience

Figure 3: Proportion of the use of Hemospray as primary or salvage therapy in patients with cessation and ongoing bleeding

Figure 4: Survival depending on bleeding cessation after use of Hemospray

TABLES

Table 1: Patients clinical and biological characteristics

	n patients
Age (years) (mean +/-SD)	65 (12.2)
Sex (%)	
Male	107 (70.4)
Female	45 (29.6)
Comorbidities (%)	140 (92)
CV & pulmonary	80 (52)
CKD	23 (15.1)
Cancer	50 (32.9)
CLD	25 (16.3)
Hereditary hemostasis disorder	5 (3.3)
Other	26 (17.1)
Antiplatelet & anticoagulant medication (%)	
None	91 (59.9)
Antiplatelet only °	21 (13.8)
Anticoagulant only **	30 (19.7)
Antiplatelet & anticoagulant combined	10 (6.6)
Vital signs (mean +/-SD)	
Systolic BP*	98.79 (23.0)
Heart rate**	97.81 (22.5)
Overt bleeding signs (%)	151 (99.3)
Hematemesis	64 (42.1)
Blood in gastric tube	11 (7.2)
Hematochezia	39 (25.7)
Melenae	71 (46.7)
Combined	38 (24.8)
Vasopressive drug requirement (%)	64 (42.1)
Hemoglobin serum level (g/dL)* (mean +/-SD)	7 (1.5)
Transfusion requirement (%)	142 (93.4)
Number of required pRBC (mean +/-SD)	2.75 (0.8)
Urea serum level (mM)** (mean +/-SD)	17.59 (9.9)

SD: standard deviation; CV: cardio-vascular; CKD: chronic kidney disease; CLD: chronic liver disease; ASA: Aspirin; BP: blood pressure; pRBC: packed red blood cells

* lowest recorded value before the endoscopy, ** highest recorded value before the endoscopy
normal Hb : 12-18 g/dL, normal urea : 3-7 mM

° Acetylsalicylic acid, Clopidogrel, Prasugrel, Ticagrelor

°° Warfarin, Dabigatran, Rivaroxaban, Apixaban, Heparin, Fondaparinux

Table 2: Endoscopic management

	n procedures (%)
Prior endoscopy (within 30 days prior)	46 (30.1)
Prior hemostatic technics	26 (17)
Epinephrine injection	12
Metal clips	8
Cautery***	4
Band ligation	4
Glue	0
Sclerotherapy	0
Hemospray	6
Cause of bleeding	
PUD (Forrest Ia and Ib)	73 (47.7)
Tumor	34 (22.2)
Esophagitis	19 (12.4)
Dieulafoy lesion	2 (1.3)
Portal hypertension	7 (4.6)
Vascular lesions*	3 (1.9)
Post endoscopy**	9 (5.9)
Ischemia (esophagus, stomach and colonic)	8 (5.2)
Mallory Weiss syndrome	1 (0.7)
Anastomotic bleeding	4 (2.6)
Other	4 (2.6)
Origin of bleeding	
Esophagus	35 (22.9)
GEJ	10 (6.5)
Body of stomach	37 (24.1)
Antrum	19 (12.4)
Duodenal bulb	45 (29.4)
Second part of the duodenum	17 (11)
Other site of bleeding	16 (10.5)
Multiple sites of bleeding	23
Type of bleeding	
None active	4 (2.6)
Oozing	129 (84.3)
Spurting	17 (11.1)
Undetermined	3 (2)
Hemospray use	
Primary therapy	60 (39.2)
Salvage therapy***	93 (60.8)
Difficulty during Hemospray application	5 (3.3)
Other hemostatic technics during the on call urgent endoscopy	
Total cases	81
Epinephrine injection	68 (44.4)
Metal clips	38 (24.8)
Thermocoagulation****	9 (5.9)
Band ligation	3 (2)
Glue	1 (0.7)
Sclerotherapy	0 (0.0)
Combined therapy	36
Bleeding cessation after Hemospray application	121 (79.0)

PUD: peptic ulcer disease; GAVE: Gastric antral vascular ectasia; GEJ: gastro-esophageal junction

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4 * GAVE, angioectasia

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6 ** endoscopic resection, biopsy, sphincterotomy

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8 *** salvage therapy was defined as the application of Hemospray® for persistent bleeding after
9 failure of other hemostatic modalities either during the same endoscopic procedure or after failure
10 of previous endoscopic attempts

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13 **** argon plasma coagulation, and bipolar electrocautery
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17 **Table 3: Patients follow-up**

	n patients or procedures (%)
Repeat endoscopy	
Total number of patients	71 (48.0)
≤ 3 days	37
≤ 30 days	17
≤ 3 and ≤ 30 days	17
Total number of repeat EGDs	88
Repeat EGD with treatment	48
Repeat EGD without treatment	40
Repeat hemostatic treatment	39 (26.4)
Epinephrine injection	13
Metal clips	21
Thermocoagulation*	8
Band ligation	1
Glue	2
Sclerotherapy	1
ERCP	1
Hemospray	12
Combined therapy	16
Non-endoscopic hemostatic treatment	34 (23.0)
Arterial embolization	14
Surgery	13
Arterial embolization and surgery	4
Radiation therapy	3
Hemospray complication	
None	148 (99.3)
Perforation	1 (0.7)
Embolus	0 (0.0)
Survival at day 30	106 (71.6)

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56 EGD: esogastroduodenoscopy, ERCP: endoscopic retrograde cholangiopancreatography

57 * argon plasma coagulation, and bipolar electrocautery
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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses

Continued on next page

Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

HIGHLIGHTS

- Real life use of the hemostatic powder Hemospray[®], in the setting of urgent endoscopic procedures performed outside working hours, by mobile on-call endoscopists, has yet to be described.
- The use of Hemospray[®] by our group was stable after becoming available and did not increase with the endoscopists experience.
- Hemospray[®] was mostly used for upper GIB (95.0%), nearly half of which were due to PUD (47.7%).
- Hemospray[®] was used as salvage therapy in 60.8% of cases. During follow up, 39.9% had a recurrence. At 30 days of follow-up, the mortality rate was 28.4%.
- 40.5% of our patients did not require a further intervention and were alive at day 30 of follow-up, despite being severely ill.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships, which may be considered as potential competing interests:

Dr Marine Camus is a consultant for Boston Scientific and Cook Medical.

Dr Xavier Dray has acted as a consultant for Alfasigma, Bouchara Recordati, Boston Scientific, Fujifilm, Medtronic, and Pentax. Author Xavier Dray is also cofounder and shareholder of company Augmented Endoscopy.

Dr Maximilien Barret is a consultant for Norgine and Medtronic.

Drs Aymeric Becq, Charles Houdeville, My-Linh Tran Minh, Nils Steuer, David Danan, Marie Anne Guillaumot, Einas Abou Ali, Aurélien Amiot, Nicolas Carbonell, Philippe Marteau and Ulriikka Chaput have no conflicts of interest or financial ties to disclose.



FIGURE 2: Use of Hemospray depending on endoscopist experience

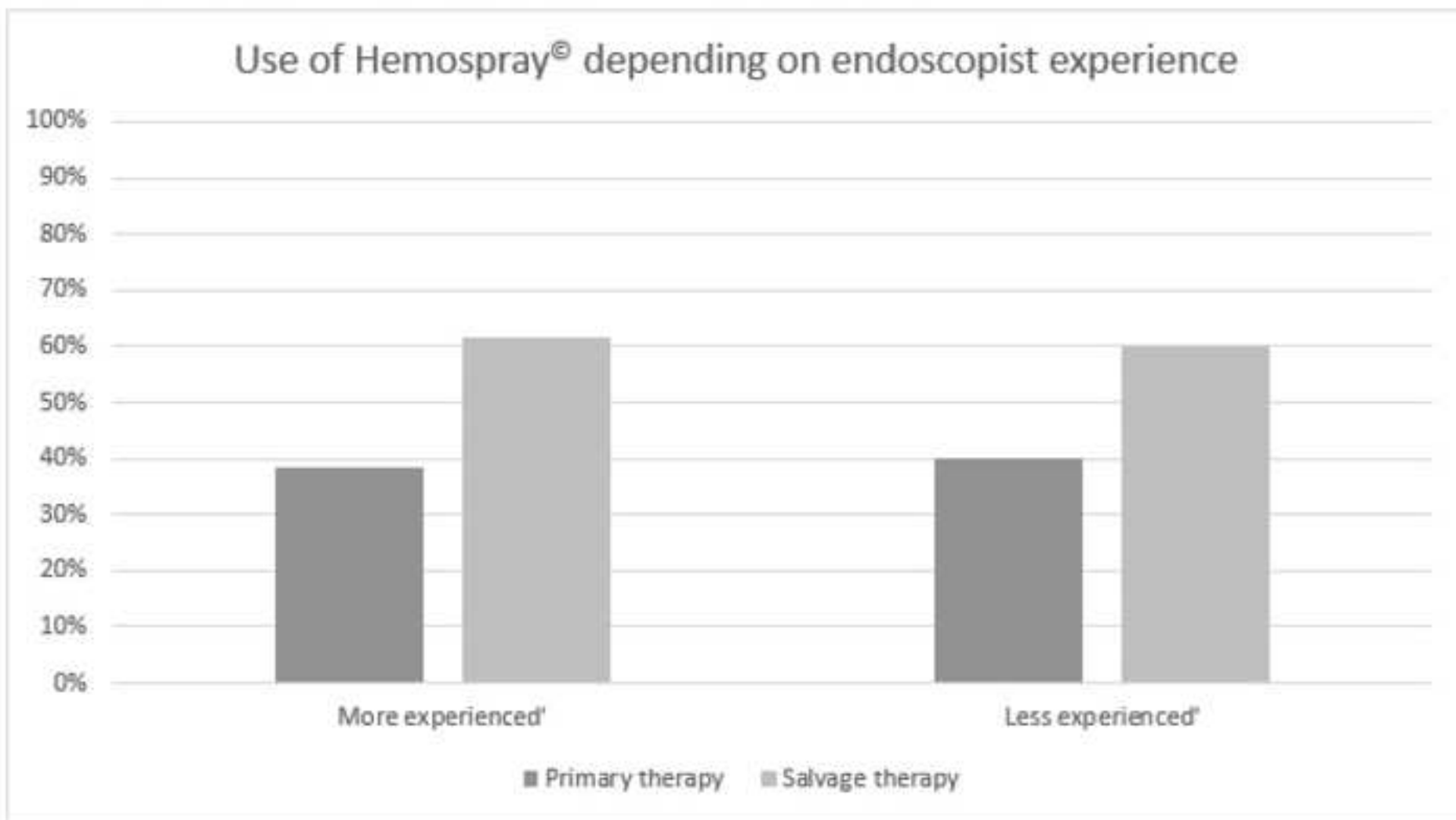


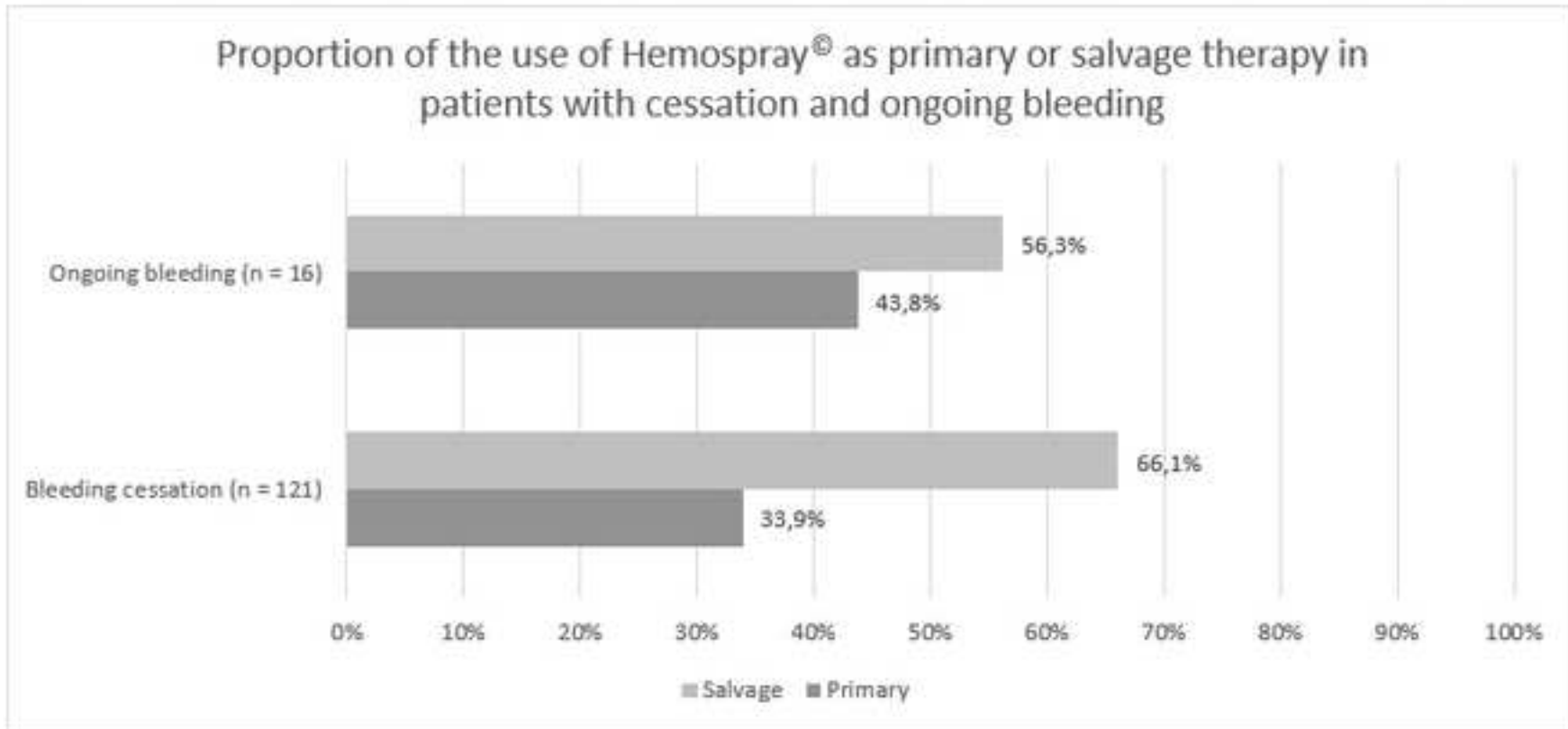
FIGURE 3: Proportion of the use of Hemospray as primary or salvage therapy in patients with cessation and ongoing bleeding

FIGURE 4: Survival depending on bleeding cessation after use of Hemospray