



High Prevalence of Upper Digestive Hemorrhages at Perpignan Hospital, Much Higher than in the Rest of France

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Abstract

The main purpose of this ancillary study of SANGHRIA was to explain why there were so many inclusions in SANGHRIA in Perpignan.

Introduction

In 2005 a multicenter prospective survey of the National Association of Gastroenterologists of General Hospitals (ANGH) had shown that ulcerative disease and portal hypertension were the main causes of high digestive hemorrhages (respectively 38 and 24.5%) with a recurrence rate of 9.9% and a mortality rate still high at 8.3% [1]. Endoscopy was performed within 24 h in 79% of cases and haemostatic movement was performed only in 66% of cases where it was indicated for ulcerative hemorrhages and 62.5% for hemorrhages on portal hypertension. The independent predictors of hemorrhagic recurrence were a hemoglobin level of 10 g/dl, a high Rockall score, low blood pressure and stigma of recent bleeding. The independent predictors of mortality were Rockall's score, comorbidities, and low blood pressure. The presence of an operator's assistant was associated with a lower rate of second endoscopy and recurrent bleeding but did not affect the endoscopic treatment rate or recidivism rate. An ancillary study showed that the mortality of ulcerative hemorrhages appeared to decline in connection with better prevention, better adherence to therapeutic recommendations and better management of comorbidities [2]. Another ancillary study focusing on the population over the age of 74 showed that the causes of hemorrhages were different from the younger population (more ulcerative hemorrhages and drug causes) [3]. There was no difference in recidivism or early mortality despite higher rates of transfusion and surgery and longer stay.

In the last 10 years, many changes have taken place with the arrival of direct oral anticoagulants such as dabigatran or rivaroxaban [4,5], and new international recommendations [6], European and French [7,8]. The purpose of conducting a new study 10 years after the first study is to study whether epidemiology, risk factors, endoscopic management and follow-up on recommendations have changed. Have incentives for better prevention of digestive hemorrhages and new anticoagulants changed the epidemiology or risk factors? Is the widest dissemination of endoscopic hemostasis techniques, the improvement of practices (development of strain or endoscopy guard, endoscopic aids) real and has it changed the prognosis of hemorrhages?

This is why a clinical observatory called SANGHRIA (ANGH High Digestive Bleeding Discounted Incidence Register) on high digestive hemorrhages was initiated by ANGH in November 2017, the main results of which are detailed in Box 1.

In this observatory, the team of Perpignan Hospital came largely at the top of the number of inclusions: 430 inclusions in Perpignan out of a total of 2,498 inclusions, or more than 17% of the total inclusions. The average inclusion in our center was close to 1.5 per day with a maximum peak at 6 inclusions in 24 h. The digestive hemorrhages received in our center included all types of etiologies: Portal hypertension, gastroduodenal ulcers, esophagitis, and cancers. Why such a difference from other general hospital centers?

Methodology

The SANGHRIA study was a multicenter observational prospective study promoted by ANGH. The items studied were the data of the investigating center, the clinical-biological data of the patient,

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Table 1: Analysis of drug prescriptions in Perpignan area (2018 health insurance data).

Area	Ratio_VKA_PPI	Ratio_VKA_PPI	Ratio_NACO_PPI	Ratio_anticoagulants_PPI
Pyrénées-Orientales	50.50%	45%	50.10%	47.30%
Occitanie East	50.90%	46.40%	51.70%	48.60%

the results of the endoscopy, the immediate evolutionary follow-up and at 6 weeks. The inclusion criteria included all patients with hematemesis, melena or acute anemia with blood in the stomach (gastroscopy, naso-gastric tube) occurring outside or during hospitalization. The data collection was carried out in each center by each investigator *via* an e-CRF. We compared the data from our center with the data from the general database of the SANGHRIA study. Possible explanations could be related to the medical organization, to a difference in the inclusion circuit, to the characteristics of the population of the health basin, to local prescribing habits, different characteristics of patients with digestive bleeding.

Results

Our initial assumptions were that the possible explanations for this large difference in the number of inclusions could be related to 1) to medical organization 2) to a difference on the inclusion circuit 3) to the characteristics of the population of the health basin 4) to local prescribing habits 5) to different characteristics of our patients with digestive hemorrhage. We will detail these 5 hypotheses below.

1) For the medical organization, our establishment is the only public somatic establishment in the Department of Pyrénées-Orientales with more than 1,000 hospitalizations per day and more than 1,200 consultants per day. There was a lack and/or abandonment of the liberal sector in the management of digestive hemorrhages: 16% of the patients included had previously gone through a private emergency department without seeing a gastroenterologist. Perpignan hospital is in fact the only center for digestive hemorrhages of this territory. The 2005 to 2017 comparison requested from the Department of Medical Information showed an increase in visits to the Emergency Department of 31% but an increase in visits for digestive hemorrhages of 141%, which corresponded in gross value to an increase in the number of stays from 296 to 713. The medical team of the Hepatogastroenterology Department providing the operational call-in included 6 hospital practitioners and a specialist assistant. 2) The principal investigator of the center has been very invested in SANGHRIA as well as the endoscopy staff, but this is not exclusive of our center. However, the inclusion circuit was optimized. Endoscopy nurses systematically informed all patients. Unlike other centers, there was only one physician who included and for this purpose screened all endoscopy schedules completed, weekends and holidays included, without specific time off, nor support from the medical research unit. 3) In the characteristics of the population, the Perpignan hospital serves a departmental basin of 482,131 inhabitants (INSEE data on 1 January 2018) concentrated on the city of Perpignan (120,605 inhabitants) and its agglomeration (264,105 inhabitants). This represented 18.3% of the former Languedoc-Roussillon region, which became eastern Occitanie in 2015. The population was 3% older than the national and regional average. The over-60s accounted for 32% in the Pyrenees-Orientales against 28.5% in Occitanie and 25.6% in France while the over-75s represented 12% in the department, 10.5% in Occitanie and 9.15% in France. Poverty was high with an average income per household of €21,392 (regional €23,560, national €26,163). Alcohol and tobacco consumption were higher in Languedoc-Roussillon. There were 16.6% regular drinkers, +5.6% compared to

the national average and 35% regular smokers, +6% compared to the national average. 4) The local prescription habits, the data of which were obtained by agreement with the Primary Health Insurance Fund of the Pyrenees-Orientales (Table 1) showed a consumption of antiperspirants, NACO and AVK 2% to 3% higher than the rest of the region but with an overall PPI consumption also 3% higher. The frequency of co-prescription was similar to the regional average, at 45% and 51% by class. The consumption of NSAIDs was identical, including in co-prescription with PPI. 5) The patients included in our center showed differences only in the following items: Less intrahospital bleeding (15.6% vs. 25.3%), hemorrhage more often related to esophagitis (19% vs. 11.5%) or portal hypertension (30% vs. 19%), despite a percentage of cirrhotic patients and an average identical CHILD score, higher Charlson severity score (3.4 vs. 2), endoscopies performed less often under general anesthesia (13% vs. 31%), fewer units transfused (1.7 vs. 3.3), less frequent intrahospital recurrence (4.3% vs. 10.5%), shorter length of hospitalization (8.2 days vs. 10.2 days); only 22 cirrhotic patients out of 88 (25%) were on propranolol. Intrahospital and 6-week mortality were similar.

Discussion

Our facility has 990 beds for obstetric surgery, making it one of the 10 largest non-academic hospitals in France. The size of the Hospital Center is an important factor in the survival of digestive hemorrhage patients. In 2009, the same team published two studies on the relationship between the hospital's volume of activity, endoscopy and mortality in patients with high digestive hemorrhage [9,10]. In centers with more than 36 high hemorrhages per year, digestive endoscopy was more often performed and mortality lower but only in cases of etiology unrelated to portal hypertension. In our analysis of the data, we can try to explain as follows the increase of 141%: Increase of activity of the Hospital Center for 31%, increase of prescription of NACO, other anticoagulants and antiperspirants 3%, decrease in prescription of PPIs not noted, decrease in emergency liberal activity 21%. More precariousness and higher consumption of tobacco and alcohol could also be involved without a percentage increase in incidence being determined. Portal hypertension is the most common cause and patients less often on propranolol are factors that need to make us reflect on our hemorrhagic prevention practices.

Conclusion

Was Perpignan hospital a separate case or can local specificities explain everything? The comparative analysis of our patients compared with all the patients included in SANGHRIA showed only minor differences. Optimization of the inclusion circuit allowed the comprehensive collection of data on high digestive hemorrhages of a GHT.

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Box 1: Overall results of the SANGHRIA study (8).

Forty-three general hospitals participated in this study and included 2,498 patients; 67.1% were men. They were 68.5 years

of age \pm 16.3 years (extreme 21 years to 98 years). Cirrhosis was present in 20.9% of patients (82% alcoholic). Aspirin was taken in 28% of patients, anti-aggregants in 12% and non-steroidal anti-inflammatory drugs in 7%. Nineteen percent of patients were taking oral anticoagulant, including 56% of anti-vitamin K and 43.8% of direct anticoagulants. This involved non-hospital hemorrhages in 74.6% of cases and 25.6% intra-hospital hemorrhages. The time of arrival of patients at the hospital was in working hours in 63% of cases, 10% of patients were in shock. Endoscopy was performed in 98.2% of patients, within 24 h in 84.2% of cases (working hours in 88% of cases) and without general anesthesia in 69% of cases. Endoscopic help was available in 91.5% of procedures. Endoscopy was described as abnormal in 90% of cases, diagnosing the most likely cause of bleeding related to ulcerative disease (44.9%), portal hypertension (18.8%), peptic esophagitis (11.5%), neoplasia (4.7%), Mallory-Weiss syndrome (4.5%) and a vascular abnormality (3.3%). Among ulcerative causes, the predominant localization was duodenal (49.2%), in portal hypertension it was the esophagus (75.5%) and for tumor causes gastric localization (70.3%). Hemorrhage was active in 24.5% of patients primarily associated with peptic ulcers and portal hypertension. The endoscopy gave rise to a hemostasis gesture in 32% of cases, it was mainly in these cases ligatures (37%), and injection of adrenaline serum (35%) and installation of clips (35%). End-of-motion bleeding was stopped in 64% of cases. Recidivism occurred in 10.5% of cases within an average of 5.5 days (0 to 40). Regarding the gravity scores, Charlson's median score was 2 (IQR: 1 to 4), Blatchford's score was 11 (IQR: 7 to 13) and Rockall's score was 5 (IQR: 3 to 6). The median length of post-endoscopic hospitalization was 7 days (standard deviation 10.3). The mean total number of blood cells transfused was 2.13 (0 to 17). Surgery was used in 3% of cases, interventional radiology in 2%. Mortality was 8.6% during hospitalization (7.7%) of which 12 (17%) were directly related to bleeding. Mortality was lower in community hemorrhage compared to patients already hospitalized (5.8% vs. 16.8%, $p=0.0001$). Factors associated with hemorrhagic recurrence were intra-hospital character (OR=1.36; 95% CI: 1.03 to 1.79), Blatchford score >11 (OR=1.45; 95% CI: 1.08 to 1.94) and active hemorrhage at the time of the first endoscopy (OR=1.94; 95% CI: 1.48 to 2.55). At 6 weeks, 12% of the evaluable patients were dead. It was significantly lower in the community hemorrhage group compared to the intra-hospital hemorrhage group (9.1% vs. 22.2%; $p<0.0001$). Predictors associated with 6-week mortality were initial transfusion (OR=1.53; 95% CI: 1.04 to 2.27), Charlson score greater than 4 (OR=1.80; 95% CI: 1.31 to 2.48), Rockall score greater than 5 (OR=1.97; 95% CI: 1.39 to 2.80), the intra-hospital nature of the hemorrhage (OR=2.44; 95% CI: 1.75 to 3.40) and hemorrhagic recurrence (OR=2.59; 95% CI: 1.85 to 3.64). Compared to the 2005 work, this descriptive analysis of the SANGHRIA study makes it possible to observe some trends that must be weighed with the analysis of sub-groups of hospitalized vs. non-hospitalized populations: shorter endoscopic management time, higher rate of endoscopic treatment, relative stability of rates of hemorrhagic recurrence, surgery and mortality.

Box 2: Prognostic scores used.

Blatchford score

The score of Blatchford makes it possible to stratify the risk of reassignment and necessity of intervention in the context of a high digestive hemorrhage. The score is between 0 and 23. Patients with a score of 0 is defined as low hemorrhagic risk. It includes urea levels,

hemoglobin, blood pressure, heart rate, the notion of melena and syncope, the existence of heart failure and hepatopathy.

Score of Charlson

Charlson's score assesses the impact of co-morbidities on the probability of survival at 10 years of age and includes age, the existence or not of diabetes, myocardial infarction, congestive heart failure, obliterating arteriosclerosis of the lower limbs, stroke, dementia, chronic lung disease, connectivitis, gastroduodenal ulcer, hemiplegia (vascular and others), moderate to severe renal failure 265 $\mu\text{mol/L}$, solid tumor, leukemia, lymphoma, cirrhosis with or without bleeding, metastatic solid tumor, HIV infection with or without AIDS,

Rockall score

The Rockall score includes age, shock, comorbidities, etiological diagnosis and recent hemorrhaging stigmas.

Box 3: Forrest endoscopic classification.

I Active jet hemorrhage (arterial).

Risk of hemorrhagic recurrence: 55%. Mortality: 11%.

I b Active hemorrhage in tablecloth.

Risk of hemorrhagic recurrence: 55%. Mortality: 11%.

If recent inactive hemorrhage, visible vessel.

Risk of hemorrhagic recurrence: 40%. Mortality: 11%.

II b Recent non-active hemorrhage, adherent clot.

Risk of hemorrhagic recurrence: 22%. Mortality: 7%.

II c Recent inactive hemorrhage, pigmented spots.

Risk of hemorrhagic recurrence: 10%. Mortality: 3%.

III No signs of bleeding, crater clean.

Risk of hemorrhagic recurrence: 5%. Mortality: 2%.

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