

Journal reading

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

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Introduction

Introduction

- Acute gastrointestinal bleeding is a common emergency while the safest and most effective transfusion strategy is **still controversial**.
- Previous studies showed:
 - In critically ill patients, a **restrictive transfusion** strategy is at least as effective as a liberal strategy.
 - Transfusion may be harmful in patients with **hypovolemic anemia**.
 - In animals, transfusion can be harmful with bleeding from **portal hypertensive** sources.

Methods

Methods

- 2003/06 through 2009/12 patients with UGIB
 - over 18 y/o** in Hospital de la Santa Creu i Sant Pau in Barcelona
- Diagnosis of UGIB:
 - Patients had **hematemesis** (or bloody NG aspirate), **melena**, or both, confirmed by hospital staff
- Patients were excluded if:
 - Patient declined transfusion
 - Massive bleeding
 - ACS, stroke, TIA, symptomatic peripheral vasculopathy
 - Transfusion within the previous 90 days
 - Recent history of trauma or surgery
 - Lower gastrointestinal bleeding
 - Clinical Rockall score of 0 with Hb level >12 g/dL

Methods

- Transfusion strategy:

	Restrictive-strategy	Liberal-strategy
Threshold for transfusion	7 g/dL	9 g/dL
Target post-transfusion Hb	7-9 g/dL	9-11 g/dL

- In both groups, **1 unit** of red cells was transfused initially
- Only prestorage **leukocyte reduced** units of packed red cells were used

- The protocol was applied until discharge or death.
- The protocol allowed for a transfusion **any time** if:
 - symptoms or signs related to anemia developed
 - massive bleeding
 - surgical intervention required
- Hb levels were measured **Q8H in first 2 days** and **QD thereafter**, and also assessed when further bleeding was suspected.

Methods

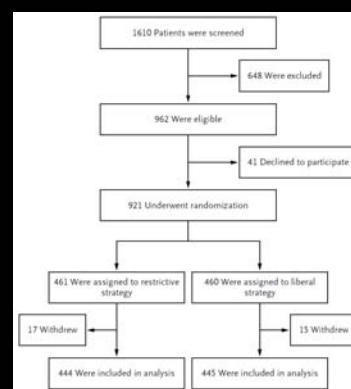
- Randomization
 - Performed with computer-generated random numbers, with sealed envelopes
 - Stratified according to the presence or absence of liver cirrhosis
- Treatment
 - All patients underwent emergency gastroscopy in first 6 hours
 - nonvariceal lesion → injection of adrenaline + electrocoagulation or endoscopic clips
 - peptic ulcer → High dose PPI for 3 days, then shifted to oral form
 - portal hypertension → band ligation or sclerotherapy, somatostatin + abx with norfloxacin or ceftriaxone for 5 days, portal pressure measured within the first 48 hours and again 2 to 3 days later

Methods

- Primary outcome
 - Rate of death from any cause within the first 45 days
- Secondary outcome
 - Rate of further bleeding
 - Rate in-hospital complications
- Statistical analysis
 - Estimated 430 patients in each group, the study would have the power to detect a between-group difference
 - Assuming 10% mortality in the liberal-strategy group, $\alpha=0.05$, $\beta=0.2$
 - Actuarial probabilities were calculated with the use of Kaplan–Meier method.
 - A Cox proportional-hazards regression model was used to compare the two transfusion-strategy groups
 - The hazard ratios and their 95% CI were calculated.

Results

Results



Results

Table 1. Baseline Characteristics of the Patients.^a

Characteristic	Restrictive Strategy (N = 444)	Liberal Strategy (N = 445)	P Value
In-hospital bleeding — no. (%)†	20 (5)	30 (7)	0.19
Rockall score‡	5.3±2.0	5.4±1.7	0.18
Source of bleeding — no./total no. (%)			
Peptic ulcer	228/444 (51)	209/445 (47)	49.1%
Location			0.95
Gastric	76/228 (33)	71/209 (34)	
Duodenal	143/228 (63)	131/209 (63)	
Stomal	9/228 (4)	7/209 (3)	
Stigmata			0.93
Active bleeding	35/228 (15)	33/209 (16)	
Visible vessel	127/228 (56)	119/209 (57)	
Gastroesophageal varices	101/444 (23)	109/445 (24)	23.6%
Mallory–Weiss tears	25/444 (6)	30/445 (7)	0.49
Erosive gastritis or esophagitis	38/444 (9)	29/445 (7)	0.26
Neoplasms	16/444 (4)	20/445 (4)	0.50
Other	36/444 (8)	48/445 (11)	

Results

Table 1. Baseline Characteristics of the Patients.^a

Characteristic	Restrictive Strategy (N = 444)	Liberal Strategy (N = 445)	P Value
Cirrhosis — no. (%)	139 (31)	138 (31)	31.1%
Alcoholic cause — no./total no. (%)	63/139 (45)	62/138 (45)	0.49
Child–Pugh class — no./total no. (%)§			0.57
A	37/139 (27)	30/138 (22)	
B	76/139 (55)	79/138 (57)	
C	26/139 (19)	29/138 (21)	
HVPG — mm Hg¶	20.1±4.4	20.6±5.2	0.61
Causes of bleeding — no./total no. (%)			
Esophageal varices	93/139 (67)	97/138 (70)	68.6%
Gastric varices	8/139 (6)	12/138 (9)	0.36
Peptic lesions	21/139 (15)	18/138 (13)	0.73

The mean score of Child–Pugh was 11.9 ± 7 in the restrictive-strategy group and 12.1 ± 6 in the liberal-strategy group ($P = 0.95$)

Results

Table 2. Hemoglobin Levels, Transfusions, and Cointerventions.^a

Variable	Restrictive Strategy (N=444)	Liberal Strategy (N=445)	P Value
Hemoglobin level — g/dl			
At admission	9.6±2.2	9.4±2.4	0.45
Lowest value during hospital stay	7.3±1.4	8.0±1.5	<0.001
At discharge†	9.2±1.2	10.1±1.0	<0.001
At day 45	11.6±1.7	11.7±1.8	0.67
Patients with lowest hemoglobin <7 g/dl — no. (%)	202 (45)	81 (18)	<0.001
Patients with lowest hemoglobin >9 g/dl — no. (%)	55 (12)	67 (15)	0.28

Results

Table 2. Hemoglobin Levels, Transfusions, and Cointerventions.^a

Variable	Restrictive Strategy (N=444)	Liberal Strategy (N=445)	P Value
Red-cell transfusion			
Any — no. of patients (%)	219 (49)	384 (86)	<0.001
Units transfused — no.			
Total‡	671	1638	<0.001
Mean/patient	1.5±2.3	3.7±3.8	<0.001
Median	0	3	<0.001
Range	0–19	0–36	
During index bleeding§	1.2±1.8	2.9±2.2	<0.001
Transfusion not adjusted to hemoglobin level — no. of patients (%)¶	35 (8)	12 (3)	0.001
Major protocol violation — no. of patients (%)‡	39 (9)	15 (3)	<0.001

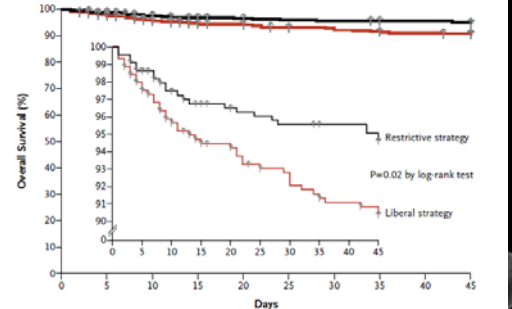
Results

Table 2. Hemoglobin Levels, Transfusions, and Cointerventions.^a

Variable	Restrictive Strategy (N=444)	Liberal Strategy (N=445)	P Value
Duration of storage of red cells — days ^{¶¶}			0.95
Median	15	15	
Range	1–40	1–42	
Fresh-frozen plasma transfusion — no. of patients (%)††	28 (6)	41 (9)	0.13
Platelet transfusion — no. of patients (%)‡‡	12 (3)	19 (4)	0.27
Crystalloids administered within first 72 hr — ml	5491±3448	5873±4087	0.19
Receipt of colloids — no. of patients (%)	86 (19)	93 (21)	0.62

Results

A Survival, According to Transfusion Strategy



Results

B Death by 6 Weeks, According to Subgroup

Subgroup	Restrictive Strategy no. of patients/total no. (%)	Liberal Strategy no. of patients/total no. (%)	Hazard Ratio (95% CI)	P Value
Overall	23/444 (5)	41/445 (9)	0.55 (0.33–0.92)	0.02
Patients with cirrhosis	15/139 (11)	25/138 (18)	0.57 (0.30–1.08)	0.08
Child–Pugh class A or B	5/113 (4)	13/109 (12)	0.30 (0.11–0.85)	0.02
Child–Pugh class C	10/26 (38)	12/29 (41)	1.04 (0.45–2.37)	0.91
Bleeding from varices	10/93 (11)	17/97 (18)	0.58 (0.27–1.27)	0.18
Bleeding from peptic ulcer	7/228 (3)	11/209 (5)	0.70 (0.26–1.25)	0.26

Results

Table 3. Study Outcomes.^a

Outcome	Restrictive Strategy (N=444)	Liberal Strategy (N=445)	Hazard Ratio with Restrictive Strategy (95% CI)	P Value
Death from any cause within 45 days — no. (%)	23 (5)	41 (9)	0.55 (0.33–0.92)	0.02
Further bleeding — no. of patients/total no. (%)				
Overall	45/444 (10)	71/445 (16)	0.62 (0.43–0.91)	0.01
Patients with cirrhosis	16/139 (12)	31/138 (22)	0.49 (0.27–0.90)	0.02
Child–Pugh class A or B	12/113 (11)	23/109 (21)	0.53 (0.27–0.94)	0.04
Child–Pugh class C	4/26 (15)	8/29 (28)	0.58 (0.15–1.95)	0.33
Bleeding from esophageal varices	10/93 (11)	21/97 (22)	0.50 (0.23–0.99)	0.05
Rescue therapies				
Balloon tamponade	3/139 (2)	11/138 (8)		0.03
TIPS	6/139 (4)	15/138 (11)		0.04
Patients with bleeding from peptic ulcer	23/228 (10)	33/209 (16)	0.63 (0.37–1.07)	0.09
Rescue therapies				
Second endoscopic therapy	20/228 (9)	26/209 (12)		0.21
Emergency surgery	4/228 (2)	12/209 (6)		0.04
No. of days in hospital	9.6±8.7	11.5±13.8		0.01

Results

Table 3. Study Outcomes.^a

Outcome	Restrictive Strategy (N = 444)	Liberal Strategy (N = 445)	Hazard Ratio with Restrictive Strategy (95% CI)	P Value
Adverse events — no. (%)				
Any ^b	179 (40)	214 (48)	0.73 (0.56–0.95)	0.02
Transfusion reactions	14 (3)	38 (9)	0.35 (0.19–0.65)	0.001
Fever	12 (3)	16 (4)	0.74 (0.35–1.59)	0.56
Transfusion-associated circulatory overload	2 (<1)	16 (4)	0.06 (0.01–0.45)	0.001
Allergic reactions	1 (<1)	6 (1)	0.16 (0.02–1.37)	0.12
Cardiac complications ^c	49 (11)	70 (16)	0.64 (0.43–0.97)	0.04
Acute coronary syndrome ^d	8 (2)	13 (3)	0.61 (0.25–0.49)	0.27
Pulmonary edema	12 (3)	21 (5)	0.56 (0.27–1.12)	0.07
Pulmonary complications	48 (11)	53 (12)	0.89 (0.59–1.36)	0.67
Acute kidney injury	78 (18)	97 (22)	0.78 (0.56–1.08)	0.13
Stroke or transient ischemic attack	3 (1)	6 (1)	0.49 (0.12–2.01)	0.33
Bacterial infections	119 (27)	135 (30)	0.87 (0.63–1.21)	0.41

Discussion

Discussion – primary outcome

- With a restrictive transfusion strategy, the outcome of **survival rate** improved probably due to better control of
 - Further bleeding
 - The need for rescue therapy
 - Serious adverse events
- Our results are consistent with previous observational studies and randomized trials performed in other settings

Discussion – compare with previous studies

- Current international guidelines recommend decreasing the Hb threshold for transfusion from 10 to 7 g/dL in GI bleeding patients,
 - based on patients with **normovolemic anemia** due to acute bleeding
 - excluded factors such as **hemodynamic instability**, **rapid onset** of anemia, or **extremely low** Hb levels
- The current study addressed the effects of transfusion in which above guidelines had excluded.

Discussion – effect on further bleeding

- These harmful effects of transfusion may be related to an impairment of hemostasis
 - Counteract the **splanchnic vasoconstrictive response** caused by hypovolemia, inducing an increased splanchnic blood flow that impair the formation of clots
 - Transfusion may also induce **abnormalities in coagulation** properties
 - induce rebound **increases in portal pressure** that may precipitate portal hypertensive related bleeding in patients of liver cirrhosis

Discussion – effect on complications

- Cardiac complications**, particularly pulmonary edema
 - More frequently with liberal transfusion strategy
 - Indicate a higher risk of **circulatory overload**
- Transfusion-related immunomodulation**, may increase the risk of complications or death
 - Unlikely to have occurred in current study given **the similar incidence** of bacterial infections in two groups
 - The universal use of prestorage **leukocytereduced red cells**

Discussion

– effect on complications

- In **Long storage blood**, storage lesions become apparent after about **14 days**
 - the median duration of storage was **15 days** in both group
 - The more use of long storage blood in the liberal-strategy group may have contributed to the worse outcome

Discussion

– Violation of strategies

- The safest and most effective transfusion strategy depends not only on the hemoglobin level but also on coexisting conditions
 - Allowed transfusions when **symptoms of anemia** developed, **massive bleeding** occurred, or **surgical intervention** required
- Violations of the transfusion protocol
 - occurred more often in the **restrictive strategy group**
 - The deviations from the protocol occurred in **less than 10%** of cases

Discussion

– Limitations

- The results **cannot be generalized** to all patients with acute gastrointestinal bleeding
 - Low risk of rebleeding were not included
 - However these patients are less likely to require transfusion
 - massive exsanguinating hemorrhage were also excluded
- The study was **not blinded**; however, bias was unlikely to introduced
 - Objective definition of the primary outcome
 - Use of a randomized design with concealed assignments

Summary

- A restrictive transfusion strategy improved the outcomes among patients with acute UGI bleeding.
 - Reduce the risk of further bleeding
 - Reduce the need for rescue therapy
 - Reduce the rate of complications
 - Increase the rate of survival was increased
- Our results suggest that in patients with acute UGI bleeding, **not performing transfusion until the Hb level falls below 7g/dL.**

Thanks
for your attention!