« Prévention de l'hémorragie digestive »

Pr Eric Maury

Médecine Intensive-Réanimation

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SORBONNE UNIVERSITÉ

1643

Liens d’intérêt

- General Electric
- Doran International
- Vygon
- Dräger
- Schulke
- Air Liquide
- Pfizer
- MSD
- Mindray
- Philips
- Sonosite fuji
- Correvio
- …

Georges Offenstadt

03/09/1944-09/04/2109

Sondage en France en Avril 2015

- 57 réanimateurs, hôpital universitaire (A: 26) et hôpital général (B: 31).

-Prescrivez vous systématiquement une prophylaxie de l'ulcère de stress chez les patients sous ventilation mécanique pour plus de 48 h ?
oui 12% A et 38.7% B (p<0.05).

-Prescrivez vous systématiquement une prophylaxie de l'ulcère de stress en cas de choc septique ? **oui 46%**

-Prescrivez vous systématiquement une prophylaxie de l'ulcère de stress chez un patient ayant un antécédent d'ulcère gastroduodénal?
Oui 77%

-**IPP prescrits dans 84% des cas**

Dans la vraie vie?

Feature Article—Continuing Medical Education

Prevention of stress ulceration: Current trends in critical care

Ryan J. Daley, PharmD; Jill A. Rebuck, PharmD, BCPS; Lynda S. Welage, PharmD, FCCP; Frederick B. Rogers, MD, FACS

Primary affiliation	
Internal medicine	221 (44.3)
Surgery	211 (42.3)
Anesthesiology	63 (12.6)
Other[b]	4 (0.8)
Yrs of critical care practice	
>12	239 (47.8)
6–12	161 (32.2)
3–5	78 (15.6)
<3	22 (4.4)
Primary area of practice	
Surgical ICU	168 (33.6)
Medical-surgical ICU	158 (31.6)
Medicine ICU	89 (17.8)
Operating room	28 (5.6)
Neurologic ICU	16 (3.2)
Trauma ICU	8 (1.6)
Burn ICU	7 (1.4)
Coronary ICU	5 (1.0)
Emergency room	2 (0.4)
Other[c]	19 (3.8)
Type of hospital	
University teaching	172 (34.4)
Community teaching	166 (33.2)
Community	121 (24.2)
Veterans Administration	15 (3.0)
Private	13 (2.6)
Other[d]	13 (2.6)
No. of ICU beds within institution	
<10	22 (4.4)
10–20	91 (18.3)
21–30	75 (15.0)
31–40	71 (14.3)
41–60	116 (23.3)
61–80	65 (13.1)
>80	58 (11.6)

519 réponses /2000

Incidence of clinically significant bleeding in the ICU, %	
<1	130 (26.1)
1–2	179 (36.0)
3–5	138 (27.7)
6–10	45 (9.0)
>10	6 (1.2)
Percent initiated on therapy for stress ulcer prophylaxis at ICU admission, %	
0	2 (0.4)
1–24	30 (6.0)
25–50	54 (10.9)
51–75	79 (15.9)
76–99	190 (38.2)
100	142 (28.6)

60% des réanimateurs intensivistes débutent une prophylaxie de l'HGDS

Crit Care Med 2004 Vol. 32, No. 10

Characteristic	All (n = 1,034)	No clinically important bleeding (n = 1,007)	Clinically importan bleeding (n = 27)
Age, years, median (IQR)	63 (48–74)	64 (48–75)	58 (51–70)
Male, gender, n (%)	576 (55.7)	562 (55.8)	14 (51.9)
SOFA score, median (IQR)	6 (4–8)	6 (4–8)	10 (7–14)
SAPS II, median (IQR)	42 (31–54)	41 (31–53)	52 (45–66)
Chronic obstructive pulmonary disease, asthma or other chronic lung disease, n (%)	205 (19.8)	201 (20.0)	4 (14.8)
Previous myocardial infarction, n (%)	101 (9.8)	99 (9.8)	4 (14.8)
Severe chronic heart failure (NYHA 3–4), n (%)	56 (5.4)	54 (5.4)	2 (7.4)
Chronic renal failure, n (%)	74 (7.2)	72 (7.1)	2 (7.4)
Liver cirrhosis or increased bilirubin (>33 µmol/l), n (%)	124 (12.0)	110 (10.9)	14 (51.9)
Metastatic cancer, n (%)	46 (4.4)	44 (4.4)	2 (7.4)
Active haematologic cancer, n (%)	36 (3.5)	34 (3.4)	2 (7.4)
AIDS, n (%)	3 (0.3)	3 (0.3)	0 (0)
Immunosuppression[b], n (%)	50 (4.8)	49 (4.9)	1 (3.7)
Coagulopathy on ICU admission[c], n (%)	128 (12.4)	118 (11.7)	10 (37.0)
Comorbidities, n (%)			
0	501 (48.5)	496 (4.9)	5 (18.5)
1	318 (30.8)	308 (30.6)	10 (37.0)
2	153 (14.8)	147 (14.6)	6 (22.2)
3	46 (4.4)	41 (4.1)	5 (18.5)
>3	16 (1.5)	15 (1.5)	1 (3.7)
Mechanical ventilation on ICU admission, n (%)	544 (52.6)	527 (52.3)	17 (63.0)
Circulatory support on ICU admission, n (%)	469 (45.4)	450 (44.7)	19 (70.3)
Renal replacement therapy on ICU admission, n (%)	70 (6.8)	61 (6.1)	9 (33.3)
Treatment with NSAID or acetylsalicylic acid prior to hospital admission, n (%)	210 (20.3)	206 (20.5)	4 (14.8)
Treatment with NSAID or acetylsalicylic acid	70 (6.8)	68 (6.8)	2 (7.4)

1 semaine, 97 ICU, 11 pays, tte nouvelle admission

Krag M; *ICM 2015;41:833-845*

Problème posé

Un peu d’histoire

1969

Respiratory Failure, Hypotension, Sepsis, and Ja

A Clinical Syndrome Associated with Lethal Hemorrhage from Acute Stress

Série de 150 patients
8 présentent une ulcération gastrique
7/8 décèdent (autopsies)

Skillman, Am J Surg 1969

8 patients présentant une HD

Patient	Location and Type of Ulcers
W. H.	Multiple gastric ulcers of fundus
R. J.	Multiple acute hemorrhagic gastric of fundus 1 to 4 cm. in size
E. Y.	No specimen available
V. T.*	Eight acute gastric ulcerations of f 0.2 to 2.0 cm. in size
R. P.	Mucosal hemorrhages and healing of fundus
J. L.*	Multiple mucosal hemorrhages an ulcerations in fundus
A. B.	Obstructing duodenal ulcer at first No specimen available after hem

Skillman, Am J Surg 1969

1978

The New England
Journal of Medicine

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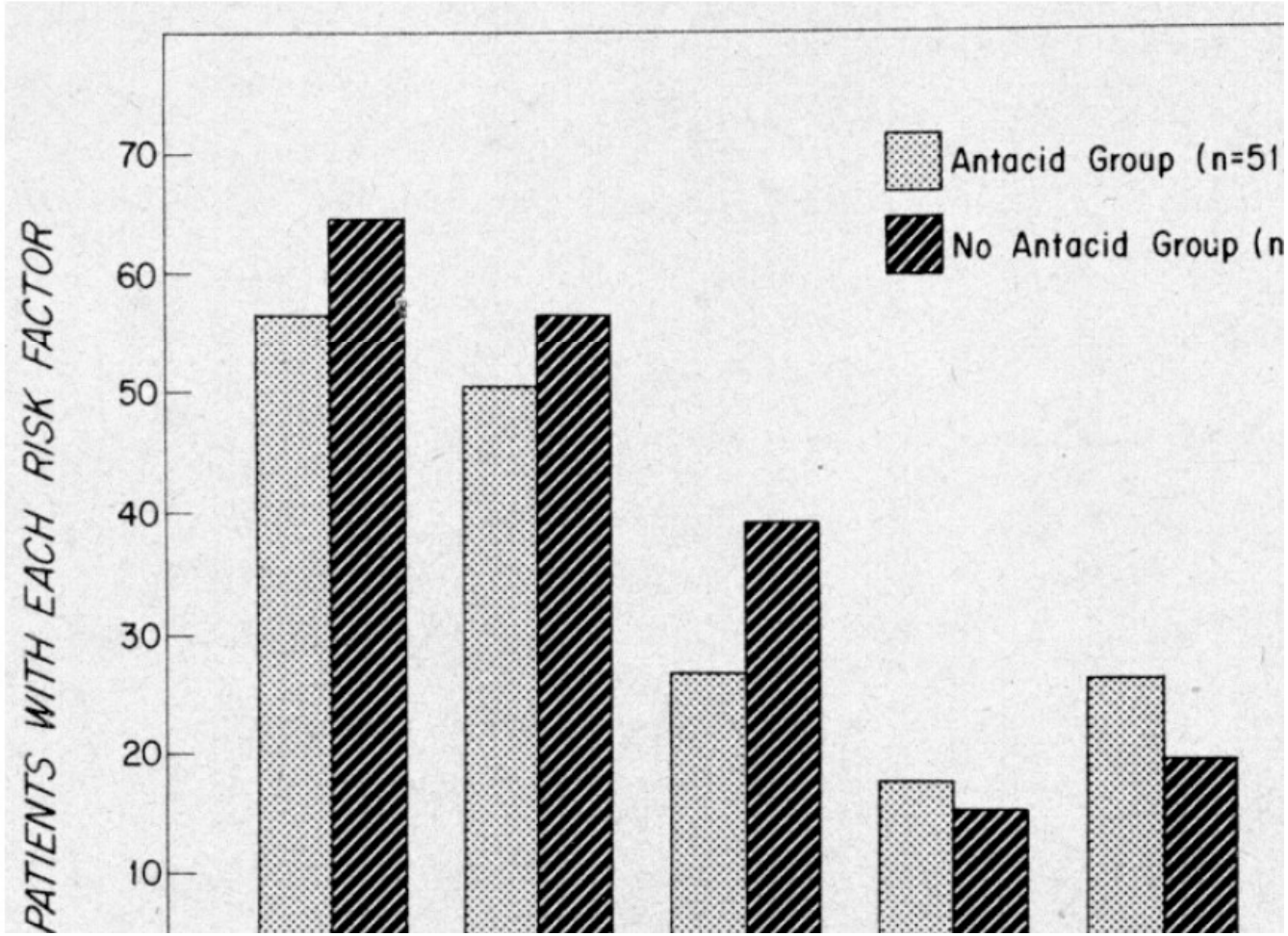
Volume 298 MAY 11, 1978

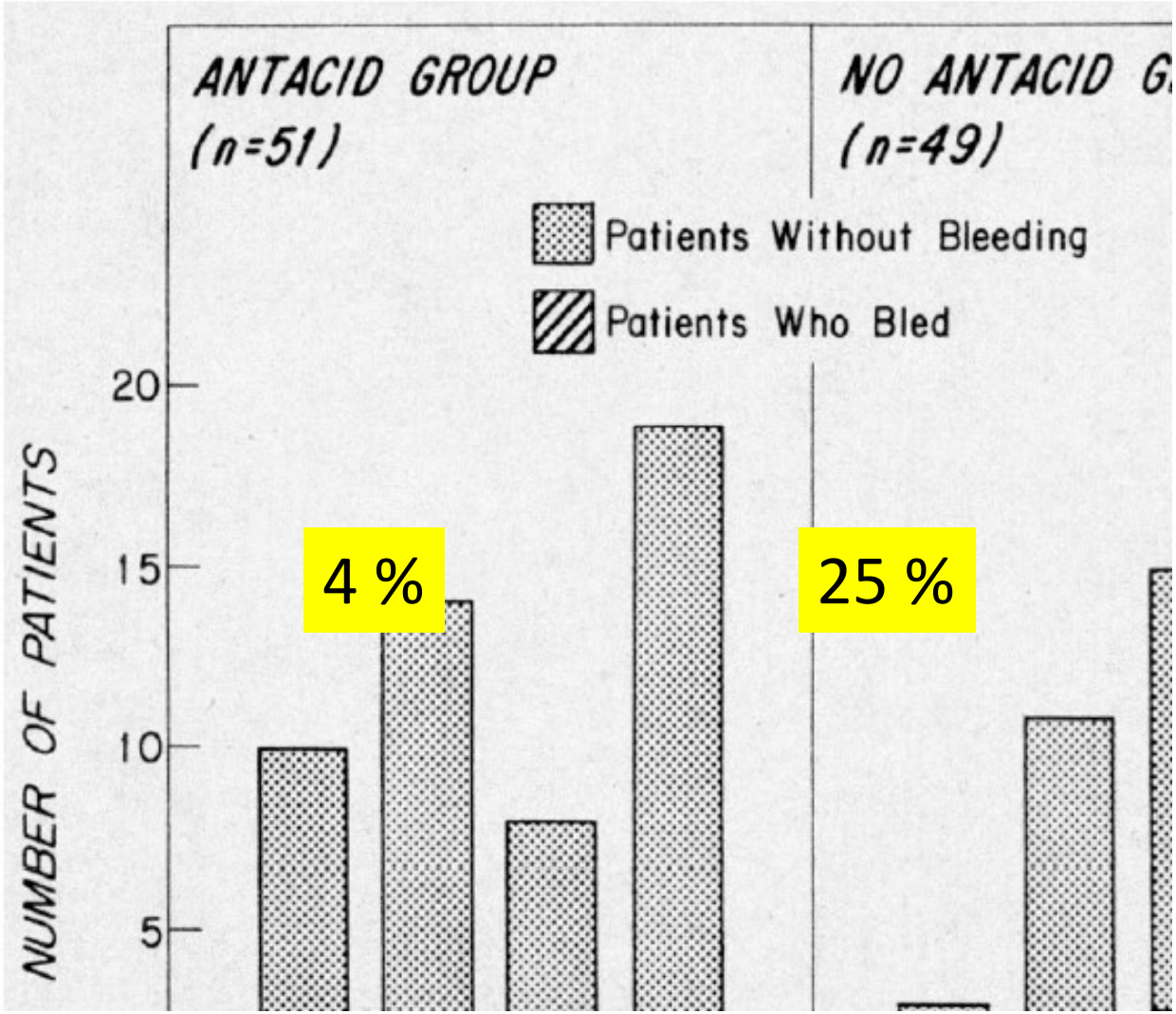
ANTACID TITRATION IN THE PREVENTION OF ACUTE GASTROINTEST

Patients de réanimation randomisés Anti-acide / Pas d'anti-acide



Hastings, NEJM 1978

Diminution des HD avec SUP



Hastings, NEJM 1978

The New England
Journal of Medicine

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Volume 298 MAY 11, 1978 Number 19

ANTACID TITRATION IN THE PREVENTION OF ACUTE GASTROINTESTINAL BLEEDING

A Controlled, Randomized Trial in 100 Critically Ill Patients

PAUL R. HASTINGS, M.D., JOHN J. SKILLMAN, M.D., LEONARD S. BUSHNELL, M.D., AND WILLIAM SILEN, M.D.

- 100 patients de réanimation
- A jeun
- Randomisation prophylaxie ou placebo
- 30 ml Aluminium hydroxyde horaire

Evaluation saignement 4 heures

Saignement 2/51 (T) vs 12/49 (P) $p<0.05$

Saignement gpe contrôle 24%!!!!!!!

The New England
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- Saignement ?

« A guaiac test was performed on the aspirate every four hours and on the stool at least once daily »

Any patient with passage of bright red blood or presence of a 4+ positive guaiaic test for three consecutive determinations

Quelle est cette maladie bizarre?

1 De quoi parle-t-on ?

2 Mécanismes de l'HD ?

3 Est-ce fréquent ?

4 Est-ce grave ?

5 Efficacité de la Prophylaxie ?

6 Tolérance de la Prophylaxie US (SUP) ?

7 Qui est encore à risque?

8 Conclusion et proposition d'algorithme

Définitions (1)

Hémorragie digestive cliniquement évidente « Overt GI Bleeding »: HD extériorisée

Hémorragie digestive cliniquement significative

- Hypotension
- Vasopresseurs
- ↘ 2 points d'hémoglobine
- Transfusion de 2 CG

Définitions (2)

Ulcère de stress ou « Stress Ulcer »

Ulcération oeso-gastro-duodénale

Liée ou non à une cause peptique

« Spécifique » du patient critique ?

« Ulcère de réanimation » terme plus juste ?

Est ce une pathologie fréquente?

	%	n	Design
Hastings 1978	14	100	RCT
Cook 1994	1.5	2252	Observationnel
Robertson 1999	80	100	Observationnel
Faisy 2003	1.8	1473	Avant après
Maury 2005	0,67	4341	Observationnel
Kantarova 2004	2,4	287	RCT
Messori 2001	6	400	Meta analyse
Marik 2001	15.8	776	Meta analyse
Krag. 2019	3,3	3298	RCT

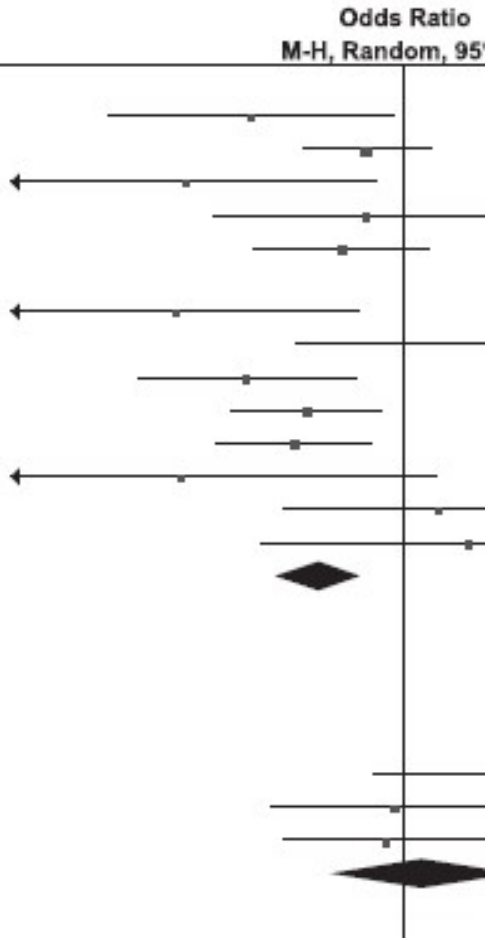
Des taux d'HGDS stupéfiants

Review Articles

Stress ulcer prophylaxis in the new millennium: A systematic review and meta-analysis

Paul E. Marik, MD; Tajender Vasu, MD; Amyn Hirani, MD; Monvasi Pachinburavan, MD

Study or Subgroup	H2RB Events	H2RB Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
1.3.1 No Enteral Nutrition							
Halloran 1980	2	26	8	24	5.6%	0.17 [0.03, 0.89]	1980
Zinner 1981	14	100	20	100	11.8%	0.65 [0.31, 1.38]	1981
Peura 1985	1	21	7	18	3.7%	0.08 [0.01, 0.72]	1985
Cheadle 1985	2	98	3	97	5.0%	0.65 [0.11, 4.00]	1985
Groll 1986	6	114	11	107	9.4%	0.48 [0.17, 1.36]	1986
Reusser 1990	0	19	0	21		Not estimable	1990
Karlstadt 1990	1	54	7	33	3.9%	0.07 [0.01, 0.60]	1990
Ruiz-Santana 1991	2	19	1	30	3.1%	3.41 [0.29, 40.50]	1991
Metz 1993	3	86	15	81	7.7%	0.16 [0.04, 0.57]	1993
Martin 1993	9	65	22	66	10.7%	0.32 [0.13, 0.77]	1993
Chan 1995	9	52	21	49	10.4%	0.28 [0.11, 0.70]	1995
Burgess 1995	0	16	5	18	2.3%	0.07 [0.00, 1.47]	1995
Hanisch 1998	3	57	2	57	4.9%	1.53 [0.25, 9.51]	1998
Kantorova 2004	2	71	1	75	3.2%	2.14 [0.19, 24.19]	2004
Subtotal (95% CI)		**798**		**776**	**81.7%**	**0.37 [0.23, 0.61]**	
Total events	54		123				
Heterogeneity: Tau² = 0.26; Chi² = 18.60, df = 12 (P = 0.10); I² = 35%							
Test for overall effect: Z = 3.90 (P < 0.0001)							
1.3.2 Enteral Nutrition							
van den Berg 1985	5	14	1	14	3.5%	7.22 [0.72, 72.70]	1985
Apte 1992	5	16	6	18	6.7%	0.91 [0.22, 3.84]	1992
Ben-menachen 1994	5	100	6	100	8.1%	0.82 [0.24, 2.79]	1994
Subtotal (95% CI)		**130**		**132**	**18.3%**	**1.26 [0.43, 3.70]**	
Total events	15		13				



Crit Care Med 2010 Vol. 38, No. 11

Comment fait-on le diagnostic ?

The New England
Journal of Medicine

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Volume 298 MAY 11, 1978 Number 19

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- Saignement ?

« A guaiac test was performed on the aspirate every four hours and on the stool at least once daily »

Any patient with passage of bright red blood or presence of a 4+ positive guaiaic test for three consecutive determinations

Hémorragie cliniquement significative

A COMPARISON OF SUCRALFATE AND RANITIDINE FOR THE PREVENTION OF UPPER GASTROINTESTINAL BLEEDING IN PATIENTS REQUIRING MECHANICAL VENTILATION

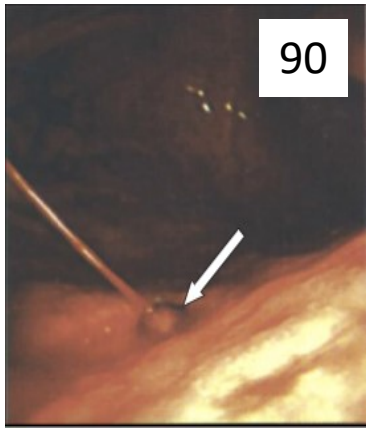
DEBORAH COOK, M.D., GORDON GUYATT, M.D., JOHN MARSHALL, M.D., DAVID LEASA, M.D., HUGH FULLER, M.B., RICHARD HALL, M.D., SHARON PETERS, M.D., FRANK RUTLEDGE, M.D., LAUREN GRIFFITH, M.Sc., ALLAN MCLELLAN, M.D., GORDON WOOD, M.D., AND ANN KIRBY, M.D., FOR THE CANADIAN CRITICAL CARE TRIALS GROUP*

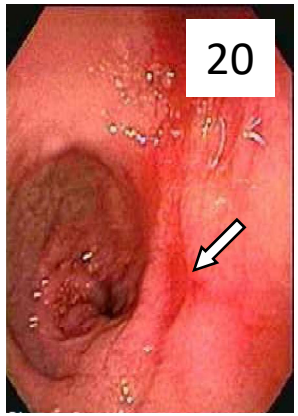
33/1200 hemorragies 10/596 (R) et 23 /604 (S)
Endoscopie 17 /33 patients
Source non retrouvée 19/33 malgré laparotomie,angiographie..

PATIENT NO.	INDICATION OF BLEEDING	FEATURES PRESENT†	TESTS OR PROCEDURES PERFORMED	SOURCE OF BLEEDING
Sucralfate group				
1	Melena	3, 4	Endoscopy	Gastric erosions
2	Melena	1, 3	Endoscopy	Gastric ulcer
3	Melena	1	Endoscopy	Gastric erosions
4	Melena	4	Endoscopy	Gastric erosions
5	Blood and coffee-grounds material in nasogastric aspirate	4	Endoscopy	Gastric erosions
6	Hematemesis, blood and coffee-grounds material in nasogastric aspirate	3, 4	Endoscopy	Gastroesophageal ulcer, gastric erosions, duodenal erosions
7	Melena	4	Endoscopy, computed tomography	Gastric ulcer, duodenal ulcer, aortic graft–enteric fistula
8	Coffee-grounds material in nasogastric aspirate, melena	1, 4	Endoscopy	Gastric erosions
9	Melena	1	Endoscopy	Esophageal ulcer, gastric erosions
10	Melena	1, 4	Endoscopy	Esophageal erosions, gastric ulcer
Ranitidine group				
11	Blood and coffee-grounds material in nasogastric aspirate, melena, hematochezia	3	Red-cell scanning, angiography, surgery	Gastric erosions
12	Hematemesis, melena, hematochezia	1	Endoscopy	Gastric erosions
13	Coffee-grounds material in nasogastric aspirate, melena	3	Endoscopy	Esophageal ulcer, duodenal ulcer
14	Melena	1	Endoscopy	Esophageal erosions, esophageal ulcer, gastric erosions

NEJM 1998;338:791-7

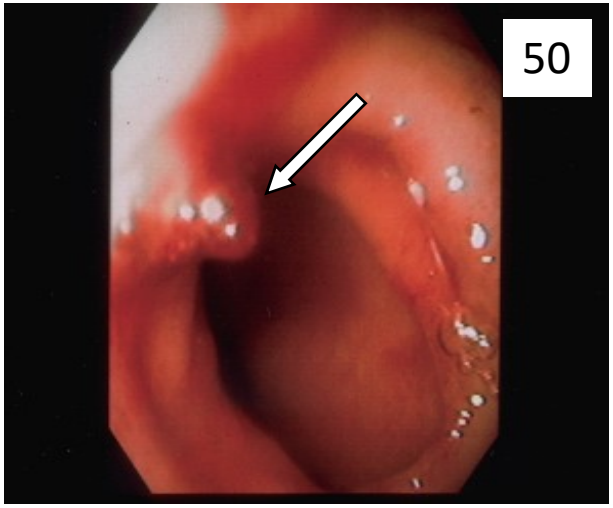
Forrest I
ACTIF

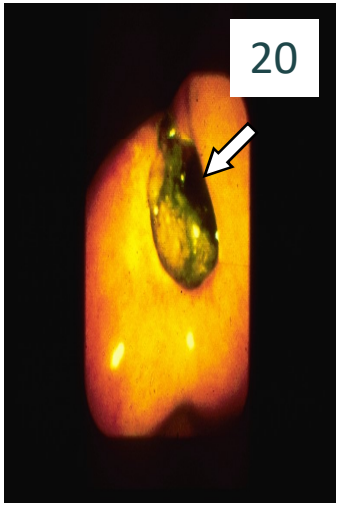


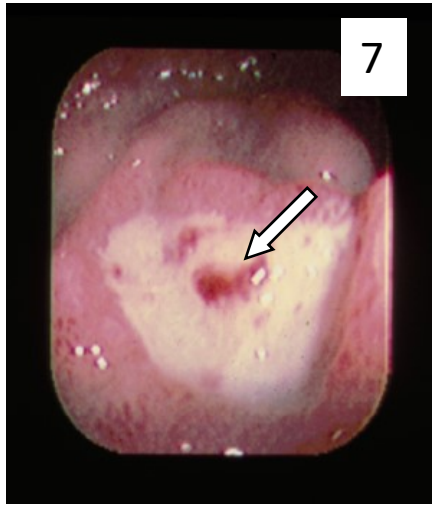


HAUT RISQUE
Traitement endoscopique
USC/USI

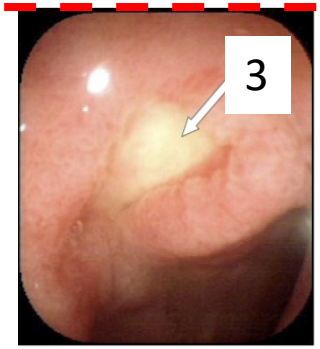
Forrest II
RECENT







Forrest III
ANCIEN



Forrest, Lancet 1974

RESEARCH

Clinical impact of upper gastrointestinal endoscopy in critically ill patients with suspected bleeding

Sylvain Jean-Baptiste[1] Jonathan Messika[1,2,3†] David Hajage[4,5,6,7†] Stéphane Gaudry[1,6,7] Ju

---

Acute anemia

Digestive bleeding

Vomiting

Hemodynamic instability

Jean-Baptiste, AIC 2018

Anomalies dans 70%
Grande hétérogénéité

Normal

Esophagitis or gastritis

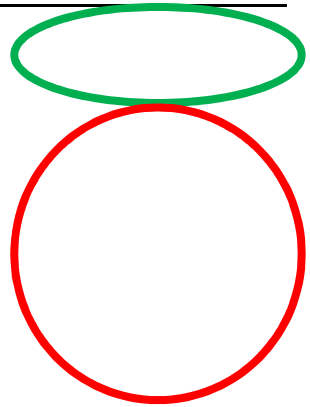
Nasogastric tube erosion

Peptic ulcer

Esophagogastric varices

Amyloidosis

Esophageal candidosis

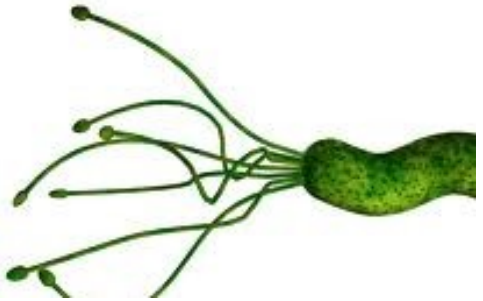


Jean-Baptiste, AIC 2018

Est-ce grave?

An observational study of upper gastrointestinal bleeding in intensive care units: Is *Helicobacter pylori* the culprit?*

Eric Maury, MD, PhD; Jacques Tankovic, MD, PhD; Anne Ebel, MD; Georges Offenstadt, MD, for the Parisian Group of the Upper Gastrointestinal Bleeding Survey



Variable	Patients With UGIB	Patients Without UGIB	*p* Value
n	29	4,312	
Mean age, yrs, ± SD	63 ± 17	57 ± 21	.01
Sex, no. M/F	17/12	2,647/1,665	.9
SAPS II at ICU admission	47 ± 14	36 ± 28	<.0001
Mechanical ventilation >48 hrs (%)	73.0	45.3	.006
Length of ICU stay (days)	16 ± 17	6 ± 11	<.001
ICU mortality (%)	73	16	<.001

HGDH cliniquement significatives et **endoscopiquement** prouvées
11/29 patients UGIB décèdent
Aucun décès directement lié à UGIB

Crit Care Med 2005 Vol. 33, No. 7

Efficacité de la prophylaxie

The New England
Journal of Medicine

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Volume 330 FEBRUARY 10, 1994 Number 6

RISK FACTORS FOR GASTROINTESTINAL BLEEDING IN CRITICALLY ILL PATIENTS

Deborah J. Cook, M.D., Hugh D. Fuller, M.B., Gordon H. Guyatt, M.D., John C. Marshall, M.D., David Leasa, M.D., Richard Hall, M.D., Timothy L. Winton, M.D., Frank Rutledge, M.D., Thomas J.R. Todd, M.D., Peter Roy, M.D., Jacques Lacroix, M.D., Lauren Griffith, M.S., and Andrew Willan, Ph.D., for the Canadian Critical Care Trials Group*

Quel facteur de risque?

Risk Factor	Simple Regression		Multiple Regression	
	Odds Ratio	P Value	Odds Ratio	P Value
Respiratory failure	25.5	<0.001	15.6	<0.001
Coagulopathy	9.5	<0.001	4.3	<0.001
Hypotension	5.0	0.03	3.7	0.08
Sepsis	7.3	<0.001	2.0	0.17
Hepatic failure	6.5	<0.001	1.6	0.27
Renal failure	4.6	<0.001	1.6	0.26
Enteral feeding	3.8	<0.001	1.0	0.99
Glucocorticoid administration	3.7	<0.001	1.5	0.26
Organ transplantation	3.6	0.006	1.5	0.42
Anticoagulant therapy	3.3	0.004	1.1	0.88

Patient Group and Risk Factor	Bleeding	No Bleeding	Percent with Bleeding*
All patients			
Neither	2	1403	0.1
Respiratory failure	8	384	2.0
Coagulopathy	1	191	0.5
Both	22	241	8.4
Total	33	2219	1.5
Patients who received prophylaxis			
Neither	1	282	0.4
Respiratory failure	6	157	3.7
Coagulopathy	0	64	0.0
Both	16	148	9.8
Total	23	651	3.4
Patients who did not receive prophylaxis			
Neither	1	1121	0.1
Respiratory failure	2	227	0.9
Coagulopathy	1	127	0.8
Both	6	93	6.1
Total	10	1568	0.6

Hémorragie digestive haute cliniquement significative
Mais ce n'est pas randomisé!!!

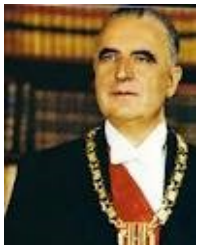
Prophylaxis vs no prophylaxis
Sucralfate /ranitidine vs nothing

Intensive Care Med (2003) 29:1306–1313
DOI 10.1007/s00134-003-1863-3

ORIGINAL

Christophe Faisy
Emmanuel Guerot
Jean-Luc Diehl
Eléonore Iftimovici
Jean-Yves Fagon

Clinically significant gastrointestinal bleeding in critically ill patients with and without stress-ulcer prophylaxis



Risk factors for CSGB	Prophylaxis (*n*=736)	No prophylaxis (*n*=737)
MV >48 h		
Number of patients	228*	284
Age (years)	65±17 (63–68)	65±18 (63–67)
SAPS II	43±19 (41–46)	46±20 (44–48)
CSGB (%)	4.4 (2–7)	2.8 (1–5)
Length of ICU stay (days)	13±12 (11–15)	14±18 (12–16)
ICU mortality (%)	32 (26–38)	32 (27–37)
Coagulopathy		
Number of patients	90*	115
Age (years)	62±20 (58–66)	64±18 (61–67)
SAPS II	42±24 (37–47)	47±27 (42–52)
CSGB (%)	5.5 (1–10)	3.5 (0–7)
Length of ICU stay (days)	9±7 (7–10)	11±19 (9–15)
ICU mortality (%)	31 (21–40)	32 (23–40)
Acute renal failure		
Number of patients	85*	116
Age (years)	70±17 (66–74)	69±17 (66–72)
SAPS II	53±25 (47–58)	57±18 (54–60)
CSGB (%)	3.5 (0–7)	3.4 (0–7)
Length of ICU stay (days)	8±6 (6–9)	11±15 (8–14)
ICU mortality (%)	43 (32–53)	56 (47–65)
MV >48 h + coagulopathy		
Number of patients	50*	77
Age (years)	61±18 (56–66)	66±16 (63–70)
SAPS II	52±26 (45–59)	55±28 (49–61)
CSGB (%)	10 (7–12)	4 (0–8)
Length of ICU stay (days)	9±8 (6–12)	15±22 (10–20)
ICU mortality (%)	46 (39–53)	45 (34–56)
MV >48 h +coagulopathy + acute renal failure		
Number of patients	20*	42
Age (years)	65±18 (57–73)	66±16 (61–71)
SAPS II	71±27 (60–83)	68±28 (60–77)
CSGB (%)	10 (−3 to +23)	7 (−1 to +15)
Length of ICU stay (days)	7±6 (5–10)	14±20 (8–20)
ICU mortality (%)	85 (69–100)	69 (55–83)

Prophylaxis vs no prophylaxis
Sucralfate /ranitidine vs nothing

Intensive Care Med (2003) 29:1306–1313
DOI 10.1007/s00134-003-1863-3

ORIGINAL

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Clinically significant gastrointestinal bleeding in critically ill patients with and without stress-ulcer prophylaxis

Cause of bleeding	Prophylaxis (n=736)	No prophylaxis (n=737)
~~Overt gastrointestinal bleeding~~	~~1.9 (0.9–2.9)~~	~~1.6 (0.7–2.5)~~
Clinically significant gastrointestinal bleeding	1.4 (1.5–2.2)	1.1 (0.3–1.8)
Confirmed extradigestive bleeding	4.6 (3.1–6.1)*	9 (7–11)
Probable extradigestive blood loss	2.2 (1.2–3.2)	3 (1.8–4.2)

SUP : Aucun effet sur la mortalité !

Alhazzani, ICM 2018

Comparison	RCTs	Direct es (95% CI) tional M	NMA estimat (95% CI)
Mortality			
H2RA vs placebo	17	0.95 (0.7	0.97 (0.77, 1.2
H2RA vs PPI	11	0.86 (0.6	0.83 (0.63, 1.1
Sucralfate vs H2RA	12	0.95 (0.7	0.96 (0.79, 1.1
Placebo vs PPI	4	0.77 (0.4	0.86 (0.62, 1.1
Sucralfate vs	6	0.98 (0.6	0.93 (0.71, 1.2

Etude observationnelle tri centrique

- 2207 patients
- IGS II: 45±21
- Femme: 42,5%
- Antécédent Ulcère gastroduodénal: 7%
- IPP à l'admission en réanimation: 16%
- Corticostéroides: 21%
- Anti agrégant (Asp/Clo/Pra): 18,2%

Guérot, Maury, Piton

Etude observationnelle tri centrique

- VM: 61%
- Sepsis sévère: 53,6%
- Vasoconstricteurs: 19,8%
- Coagulopathie: 28,9%
- Insuffisance rénale:25%
- Alimentation entérale: 81%
- SNG: 52% (aspiration 9%)
- Prophylaxie IPP :24%

Guérot, Maury, Piton

Etude observationnelle tri centrique

- Hémorragies hautes significatives endoscopiquement prouvées :65
- Hemorragies gastrodudénales: 45

2%, IC 95% [1,7-2,3]

Varices oesophagiennes	8
Oesophagite	8
Ulcère oesophagien	3
Erosion gastrique	4
Ulcère gastrique	16
Erosion duodénale	1
Ulcère duodénal	24

Guérot, Maury, Piton

Etude observationnelle tri centrique

	HGDS	Pas d'HGDS	p
IGS II	54 [19-85]	45 ± 20	0.01
Age	67	57 ± 45	0,02
Atcd Ulcère	9/45 (20%)	153/2162 (7 %)	0,003
Anti agrégant	13/45 (29%)	403/2162 (18,2%)	0,12
Sepsis sévère	30/45 (67%)	1214/2162 (56%)	0,21
VM	38/45 (84%)	1216/2162 (56%)	0,0001
Coagulopathie	18/45 (40%)	649/2162 (28%)	0,2
Vasoconstricteurs	10/45 (22%)	426/2162 (20%)	0,8
SNG	33/45 (73%)	1183/2162 (55%)	0,02
Insuffisance rénale	24/45 (53%)	557/2162 (26%)	0,001
IPP	18/45 (40%)	528/2162 (24%)	0,026

Guérot, Maury, Piton

Etude observationnelle tri centrique

- Soit 2% IC 95% [1,7-2,3]
- Incidence HGDS sous IPP: 3,4%
- Incidence HGDS sans IPP: 1,6%
- OR IPP :2,19 IC 95% [1,19-4]!!

- La prophylaxie par IPP n'est pas associée à une diminution du risque d'HGDS

Guérot, Maury, Piton

Qui est encore à risque?

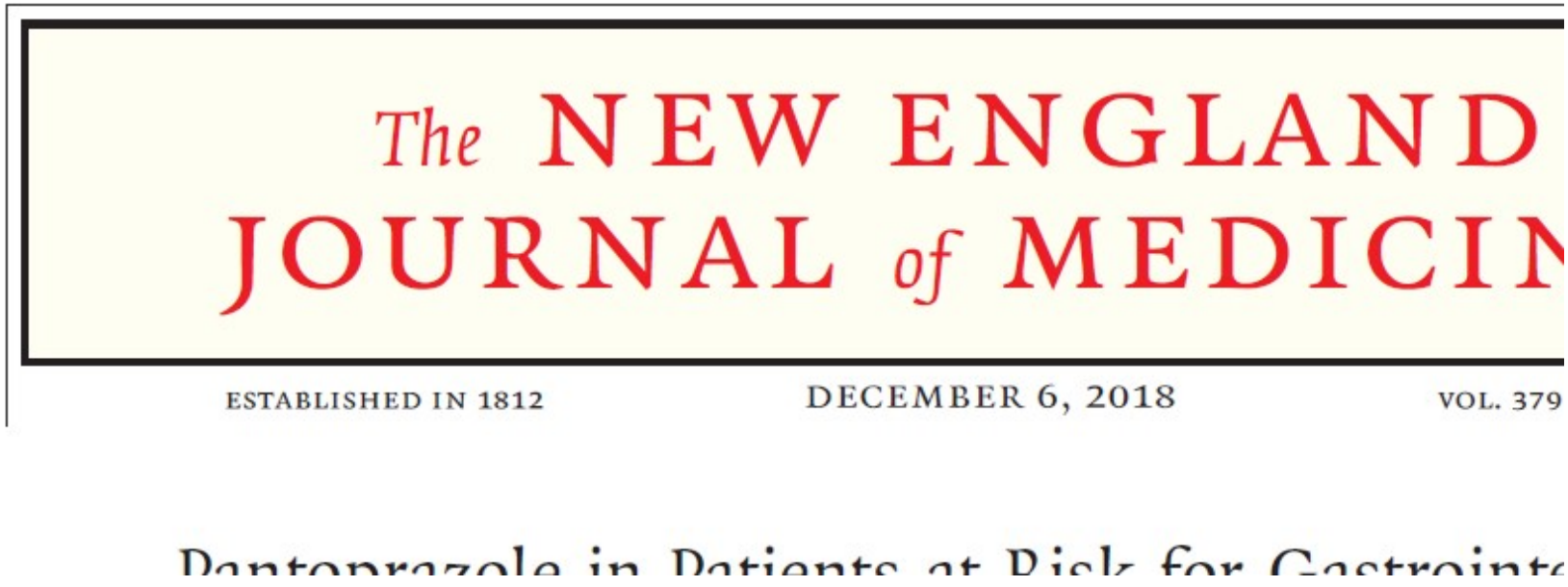
Quels patients à risque d'hémorragie ?

Score	Risk Factor I (severe)	Score	Risk Factor II (moderate)	Score	Risk Factor III (only in combination with I, II)
20	History of ulcer*	5	Transplantation	2	Relaparatomy
15	Acute renal insufficiency (creatinine >600 mg)	5	Coagulopathy	2	Ileus
15	Burn >25%	5	Neurogenic shock*	2	Hypovolemic shock
15	Sole cerebral trauma with neurologic deficit				
10	Severe infection	5	Intracranial bleeding	2	Anaphylactic shock*
10	Severe polytrauma				
10	Cardiogenic shock*	5	Transfusion (>4 units)	2	Septic shock
10	Pancreatitis	5	Age >65	2	Cerebral trauma (in combination with polytrauma)
10	Kidney disease*	3	Heparin medication	2	Corticosteroid therapy
10	Gastroenterologic disease	3	Hb <10 for >24 hours		
7	Acute renal insufficiency (creatinine 300–600 mg)	2	BP <100 for >1 hour >1 x		
7	Respiratory insufficiency	2	BP >200 for >2/days >1 x		

Tryba M, Am J Med 1987

Que faire alors?

Bénéfice de la prophylaxie??



BACKGROUND

Prophylaxis for gastrointestinal stress ulceration is frequently given to intensive care unit (ICU), but its risks and benefits are unclear.

METHODS

In this European, multicenter, parallel-group, blinded trial, we randomly who had been admitted to the ICU for an acute condition (i.e., an unpla and who were at risk for gastrointestinal bleeding to receive 40 mg of int prazole (a proton-pump inhibitor) or placebo daily during the ICU st outcome was death by 90 days after randomization.

RESULTS

A total of 3298 patients were enrolled; 1645 were randomly assigned to t group and 1653 to the placebo group. Data on the primary outcome w 3282 patients (99.5%). At 90 days, 510 patients (31.1%) in the pantoprazol (30.4%) in the placebo group had died (relative risk, 1.02; 95% confide 0.91 to 1.13; P=0.76). During the ICU stay, at least one clinically importa posite of clinically important gastrointestinal bleeding, pneumonia, C infection, or myocardial ischemia) had occurred in 21.9% of patients as prazole and 22.6% of those assigned to placebo (relative risk, 0.96; 95% In the pantoprazole group, 2.5% of patients had clinically important bleeding, as compared with 4.2% in the placebo group. The number of fections or serious adverse reactions and the percentage of days alive wit within 90 days were similar in the two groups.

Critères d'inclusion

All adult (18 years or older) patients who are acutely admitted to the ICU with one or r
following risk factors for gastrointestinal bleeding:

- Shock (continuous infusion with vasopressors or inotropes, systolic blood pres
  90 mmHg, mean arterial blood pressure below 70 mmHg or plasma lactate lev
  or above)
- Acute or chronic intermittent or continuous renal replacement therapy (RRT)
- Invasive mechanical ventilation which is expected to last more than 24 hours
- Coagulopathy (platelets below 50 × 10^9/l, or international normalized ratio (INF
  or prothrombin time (PT) above 20 s) documented within the last 24 hours
- Ongoing treatment with anticoagulant drugs (prophylactic doses excluded)
- History of coagulopathy (platelets below 50 × 10^9/l or INR above 1.5 or PT abo
  within the 6 months prior to hospital admission)

Et l’effet de la nutrition entérale?

	Pantoprazole	P
Enteral nutrition *	*no. (% of patients)* †	
Day 1	956/1644 (58.2)	9
Day 2	1176/1598 (73.6)	12
Day 3	1088/1359 (80.1)	11
Day 4	955/1145	9

Objectif primaire

Primary outcome:

90-day mortality: death from any cause within 90 days following the day o

???????

Objectifs secondaires

- Incidence des hémorragies digestives cliniquement significatives
- Pneumonies
- Infection à *Clostridium difficile*
- Infarctus du myocarde

Objectifs secondaires

Secondary outcomes:

1) Proportion of patients with one or more of the following clinically important a clinically important gastrointestinal bleeding, pneumonia, *Clostridium Difficile* i myocardial ischemia. The events are defined as follows:

Clinically important gastrointestinal bleeding: overt gastrointestinal bleeding* a the following four features within 24 hours of gastrointestinal bleeding (in the a causes) in the intensive care unit

a) spontaneous drop of systolic blood pressure, mean arterial pressure o pressure of 20 mmHg or more
b) start of vasopressor or a 20% increase in vasopressor dose

Résultats

Outcomes	Pantoprazole	Placebo	
Primary outcome: death by day 90 — no./total no. (%)	510/1642 (31.1)	499/1640 (30.4)	1.0
Secondary outcomes			
One or more clinically important events — no./total no. (%)‡	360/1644 (21.9)	372/1647 (22.6)	0.9
One or more episodes of clinically important gastrointestinal bleeding — no./total no. (%)	41/1644 (2.5)	69/1647 (4.2)	0.0
One or more infectious adverse events — no./total no. (%)§	276/1644 (16.8)	279/1647 (16.9)	0.9
Severe adverse reaction — no./total no. (%)¶	0/1644 (0)	0/1647 (0)	

. Malheureusement l'essai n'est pas construit pour évaluer séparément les évènements composant le critère de jugement secondaire. Les résultats sont donc fournis avec un odds ratio mais sans valeur de p ce qui rend l'interprétation délicate/ incertaine.

	Pantoprazole (N=1644)	
	no. (% of patients)	
Overt gastrointestinal bleeding	88/1644 (5.4)	1
Clinically important gastrointestinal bleeding	41/1644 (2.5)	6
Criteria for clinically important gastrointestinal bleeding*		
Spontaneous drop of systolic, diastolic, or mean arterial pressure of 20 mmHg or more	25/41	
Vasopressor initiated or increased by 20% or more	22/41	
Hemoglobin decrease by at least 2 g/dl (1.24 mmol/l)	23/41	
Transfusion of 2 units of packed red blood cells or more	29/41	
Intervention		
Endoscopy	16	
Surgery	3	
Coiling	2	
Source of gastrointestinal bleeding (if confirmed)		
Ulcer	10	
Gastritis	4	
Varices	0	
Other	6	

Documentation des hémorragies

	Pantoprazole (N=1644)	
	no. (% of patients)	
Overt gastrointestinal bleeding	88/1644 (5.4)	148
Clinically important gastrointestinal bleeding	41/1644 (2.5)	69
Criteria for clinically important gastrointestinal bleeding*		
Spontaneous drop of systolic, diastolic, or mean arterial pressure of 20 mmHg or more	25/41	
Vasopressor initiated or increased by 20% or more	22/41	
Hemoglobin decrease by at least 2 g/dl (1.24 mmol/l)	23/41	
Transfusion of 2 units of packed red blood cells or more	29/41	
Intervention		
Endoscopy	16	
Surgery	3	
Coiling	2	

	Pantoprazole (N=1644)	Pla (N=
	no. (% of patients)	
Overt gastrointestinal bleeding	88/1644 (5.4)	148/16
Clinically important gastrointestinal bleeding	41/1644 (2.5)	69/16
Criteria for clinically important gastrointestinal bleeding*		
Spontaneous drop of systolic, diastolic, or mean arterial pressure of 20 mmHg or more	25/41	46
Vasopressor initiated or increased by 20% or more	22/41	35
Hemoglobin decrease by at least 2 g/dl (1.24 mmol/l)	23/41	41
Transfusion of 2 units of packed red blood cells or more	29/41	39
Intervention		
Endoscopy	16	2
Surgery	3	
Coiling	2	
Source of gastrointestinal bleeding (if confirmed)		
Ulcer	10	1
Gastritis	4	
Varices	0	
Other	6	1

71 %	56 %	NS

Prise en charge par le réanimateur des hémorragies digestives de l'adulte et de l'enfant.

Recommandations formalisées d'experts
sous l'égide de la Société de Réanimation de Langue Française (SRLF),
avec la participation du Groupe Francophone de Réanimation et Urgences Pédiatriques (GFRUP),
de la Société Française de Médecine d'Urgence (SFMU),
de la Société Nationale Française de Gastroentérologie (SNFGE),
de la Société Française d'Endoscopie Digestive (SFED)

Gastrointestinal bleeding management by intensivists in adult and children.
Recommendations by an expert panel from the French society of intensive care medicine

D. Osman · M. Djibré · D. Da Silva · C. Goulenok · Groupe d'experts

Groupe d'experts : Marc Bardou (Dijon), Sophie Branchereau (Le Kremlin-Bicêtre), Christophe Bureau (Toulouse), Nicolas Carbonell (Paris), Philippe Cluzel (Paris), Emmanuel Guérot (Paris), Pierre-François Laterre (Bruxelles), Gilles Lesur (Boulogne), Emmanuel Mas (Toulouse), Eric Maury (Paris), Stéphane Nahon (Montfermeil), Philippe Otal (Toulouse), Dominique Pateron (Paris), Gaël Piton (Besançon), Jean-Pierre Quenot (Dijon), Marika Rudler (Paris), Dominique Thabut (Paris), Pierre Tissières (Le Kremlin-Bicêtre), Patrice Valleur (Paris).

Commission des référentiels et de l'évaluation de la SRLF : Cédric Bretonnière, Karim Chaoui, Aurélie Cravoisy, Michel Djibré, Laurent Dupic, Fabienne Fieux, Dominique Hurel, Virginie Lemiale, Olivier Lesieur, Martine Lesny, Pascal Meyer, Christophe Milési, Benoit Misset, Mehran Monchi, David Orlikowski, David Osman, Jean-Pierre Quenot, Daniel Da Silva, Lilia Soufir, Thierry Van Der Linden, Isabelle Verheyde

Réanimation
DOI 10.1007/s13546-012-0489-2

1 Il faut probablement considérer à risque d'HD sur ulcère gastroduodénal les pts admis en réanimation et présentant un antécédent d'ulcère gastroduodénal *(a fort)*.

2 L'alimentation entérale précoce est une mesure efficace pour prévenir l'HD sur ulcère « de stress » *(a fort)*.

3 Il faut considérer à risque d'HD sur ulcère des stress les pts justifiant d'une ventilation mécanique de plus de 48 h et ne pouvant être alimentés par voie entérale *(a fort)*.

4 Il faut considérer à risque d'HD sur ulcère des stress les pts admis en réanimation et présentant une insuffisance rénale et/ou un ttt antiagrégant plaquettaire et/ou une coagulopathie *(a fort)*.

5 Il ne faut pas réaliser de prophylaxie médicamenteuse systématique de l'ulcère de stress chez le pt de réanimation alimenté par voie entérale *(a fort)*.

6 Il faut probablement réaliser une prophylaxie antiulcéreuse systématique chez les pts de réanimation ayant un ATCD d'UGD, même alimentés par voie entérale *(a faible)*.

7 Il faut probablement réaliser une prophylaxie antiulcéreuse systématique chez les pts de réanimation ayant un ttt antiagrégant plaquettaire, même alimentés par voie entérale *(a faible)*.

8 En l'absence de nutrition entérale, il faut probablement réaliser une prophylaxie antiulcéreuse médicamenteuse chez les pts ventilés *(a faible)*.

9 En l'absence de nutrition entérale, il faut probablement réaliser une prophylaxie antiulcéreuse médicamenteuse chez les pts ayant une coagulopathie *(a faible)*.

Stress-related mucosal disease in the critically ill patient

- Prévalence de l'HGDS cliniquement pertinente (très) faible (~1%),
- Prophylaxie de l'HGDS cliniquement pertinente doit être limitée
- IPP semblent être la prophylaxie la moins mauvaise
- Prophylaxie trop utilisée
- 2/3 patients sans facteurs de risque traités, 2/3 traitements poursuivis au sortir de réanimation
- 1/3 rentrent à domicile avec un traitement
- RCT et études observationnelles nécessaires pour évaluer le stratégies préventives de l'hémorragie gastroduodénale de stress en réanimation

- Arrêter de lire aveuglément les méta analyses!!!!!!!!!

Nat. Rev. Gastroenterol. Hepatol. **12**, 98–107 (2015)

…The main aim of prophylaxis should be to prevent clinically relevant bleeding, i.e., necessitating transfusions of at least 2 U of packed RBCs. Without any specific prophylaxis, this kind of bleeding is presently exceptional in ICUs…

… Since the frequency of clinically relevant gastric bleeding is so low, it appears ethical or even warranted to perform trials with untreated control groups…

Crit Care Med 1992 ; 20 : 908

…We wonder why, in their current study, they did not include a control group that received no treatment…

N Engl J Med 1998 ; 339 : 267

…We want to point on the fact that there is another very conflicting recommendation in the Surviving Sepsis Campaign, which is the prevention of stress ulcer bleeding. In our opinion, the actual data do not permit recommending a specific prevention of stress ulcer in severe sepsis…

Crit Care Med 2008 ; 36 : 1990

… We are surprised that among the five targeting quality measures proposed by the subcommittee of Society of Critical Care, there is stress ulcer prophylaxis, which is such a debatable question…

Crit Care Med 2010 ; 38 : 1014

Hémorragies de stress plus de questions que de réponses

reanimation 2020

PARIS 5th-7th FEBRUARY

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