What To Do After Your Patient Develops Ascites

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Conflict of Interest Disclosure

(over the past 24 months)

No relevant relationships with any commercial or non-profit organizations.

CanMEDS Roles Covered

X	**Medical Expert** (as *Medical Experts*, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. *Medical Expert* is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
X	**Communicator** (as *Communicators*, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as *Collaborators*, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as *Leaders*, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
X	**Health Advocate** (as *Health Advocates*, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
X	**Scholar** (as *Scholars*, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as *Professionals,* physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Outline

- Diagnosis & Evaluation of New-Onset Ascites
- Management of Ascites in Cirrhosis / Portal Hypertension
- Controversies in Ascites Management


OAG
GAMIFICATION
Khan - Game Code:
QUIVER

Ascites - Definitions

- **Uncomplicated**
  - Grade 1 – Mild – only seen on U/S
  - Grade 2 – Moderate – moderate, symmetrical distension
  - Grade 3 – Gross – marked abdominal distension
- **Complicated -** Infected, Refractory or Associated w/ Hepatorenal Syndrome (HRS)

Ascites - Definitions

- **“Refractory”**
  - Cannot be mobilized or recurrence of which cannot be prevented by medical therapy
  - **Diuretic Resistant vs. Diuretic-Intractable**

New-Onset Ascites – So What?

- Most common decompensating event: 5-10% / year
- 5-Year survival ↓ from 80% to 30%

Causes of Ascites

PORTAL HYPERTENSION
Cirrhosis
Alcohol-associated Hepatitis
Veno-occlusive disease (BCS, SOS)
Heart Failure
Constrictive Pericarditis
HYPOALBUMINEMIA
Nephrotic syndrome
Protein Losing Enteropathy
PERITONEAL DISEASE
Malignancy (Ovarian CA., Mesothelioma)
Infectious Peritonitis (TB, Fungal)
Peritoneal Dialysis
OTHERS
Chylous Ascites, Pancreatic Ascites, Myxedema

Evaluation & Diagnosis

- **History**
- **Physical Exam**
- **Laboratory Investigations** – LFTs, BUN, Cr, Electrolytes, Urine Studies, Tests to evaluate etiology;
- **Diagnostic Paracentesis**
- **Ultrasound w/ Dopplers**

Diagnostic Paracentesis in New-Onset Ascites

- **Timing – within 12 hours!**
  - Early paracentesis → ↓ **mortality, SBP-related mortality, 30-day readmission** (Rosenblatt et al. AJG 2019)
- **Contraindications**
  - Pregnancy, DIC, Severe Bowel Distension
  - **NOTE:** Safe in coagulopathy (INR > 1.5 and Plt < 50,000) – 1% risk of bleeding* *(De Gottardi et al. CGH 2009)*

What do I analyze in ascitic fluid?

Routine	Optional	Unusual	Unhelpful
Cell count	Cytology	AFB smear	pH
Albumin	Glucose	Triglyceride	Lactate
Total Protein	LDH	Bilirubin	Cholesterol
Culture*	Amylase		Fibronectin
			Anti-trypsin

Serum-Ascites Albumin Gradient (SAAG)

SAAG ≥11 g/L	TP < 25 g/L	Cirrhosis
	TP ≥ 25 g/L	RHF, Budd-Chiari (early)
SAAG <11 g/L	TP < 25 g/L	Nephrotic syndrome

Abdominal Ultrasound w/ Dopplers

- Quick, Cheap, Easy
- Confirmation of Ascites
- Evaluate etiology (e.g. BCS, Malignancy / Mets, PVT, IVC collapse)

Beware of Complications

- **Refractory Ascites**
- **Spontaneous Bacterial Peritonitis (SBP)**
  - IV Ceftriaxone + Albumin (Day 1 and 3)
  - Secondary Prophylaxis
- **Hepatorenal Syndrome (HRS)**
  - 25% Albumin (1g/kg/day x 2 days) → Albumin (20-40 g/day) + Norepinephrine/Terlipressin/Midodrine-Octreotide/
- Umbilical Hernias

Management of Uncomplicated Ascites

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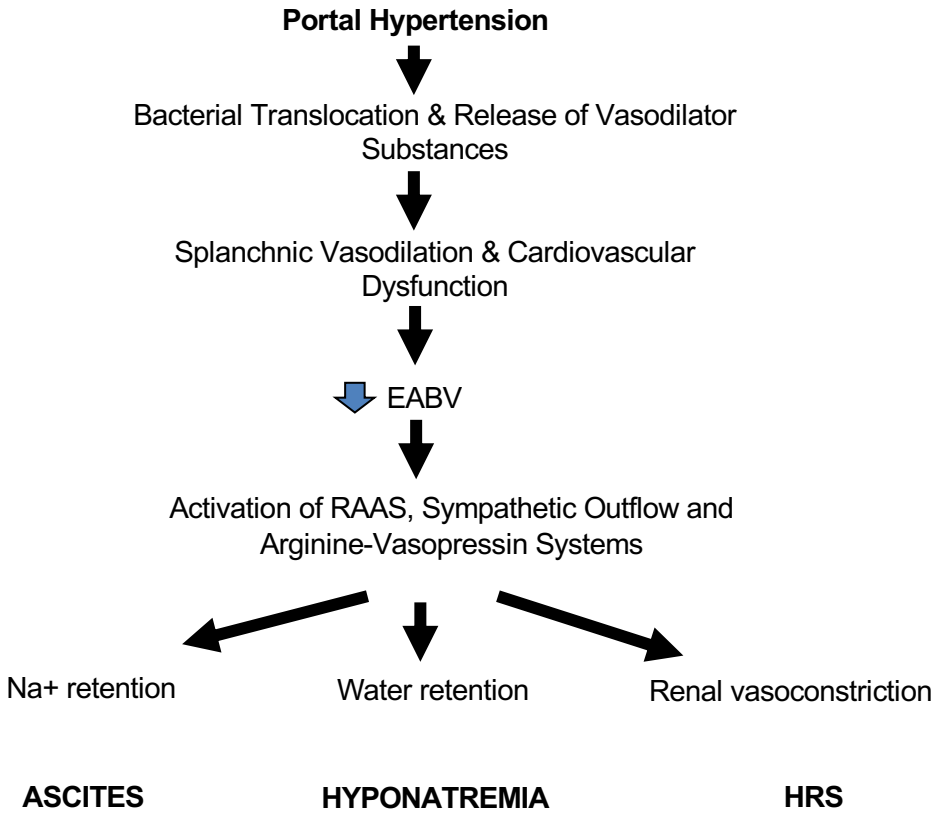
Portal Hypertension
Bacterial Translocation & Release of Vasodilator Substances
Splanchnic Vasodilation & Cardiovascular Dysfunction
EABV
Activation of RAAS, Sympathetic Outflow and Arginine-Vasopressin Systems
Na+ retention
Water retention
Renal vasoconstriction
ASCITES
HYPONATREMIA
HRS

Sodium Restriction & Diuretics

- 88 mmol / day = **2 g sodium / day**
- **Spironolactone**
  - May be sufficient alone with ↓ side effects*
  - 100 mg/day; Max: 400 mg/day
- **Loop Diuretic** (e.g. Furosemide)
  - Lowers K+; Blocks compensatory proximal tubular Na reabsorption;
  - 40 mg/day; Max: 160 mg/day

Angeli P, Gatta A, Caregaro L, Menon F, Sacerdoti D, Merkel C, et al. Tubular site of renal sodium retention in ascitic liver cirrhosis evaluated by lithium clearance. Eur J Clin Invest 1990;20:111-117. 30)
Gatta A, Angeli P, Caregaro L, Menon F, Sacerdoti D, Merkel C. A pathophysiological interpretation of unresponsiveness to spironolactone in a stepped-care approach to the diuretic treatment of ascites in nonazotemic cirrhotic patients. Hepatology 1991;14:231-236.

Sodium Restriction & Diuretics

- **Assess Response & Compliance with Spot Urine Na+/K+**
  - **> 1**: Should lose weight; if not, question compliance
  - **< 1**: Optimize diuretics
- **Look Out for and Manage Side Effects of Diuretics** (electrolyte abnormalities, cramps, HE, gynecomastia, etc.)

- **What about Fluid Restriction?**
  - Not necessary unless Na < 125 mEq/L

Large Volume Paracentesis

- **Brisk fluid reduction, ↓ LOS**
- **Complications:**
  - Post-Paracentesis Circulatory Dysfunction (Renal failure, Hyponatremia, HE, Decreased Survival)
  - **PREVENTION: 6-8 g 25% albumin / L ascitic fluid removed**

Other Management Tips

- **Avoid NSAIDS, ACE-Is, ARBs, alpha-1 adrenergic blockers, dipyridamole**
  - Reduce EABV and renal perfusion
- **Avoid nephrotoxic agents**
- **Albumin infusions?**
  - ANSWER vs. MACHT vs. ATTIRE
  - **Cannot recommend scheduled, repeated albumin infusions outside of standard indications yet.**

Controversies in Ascites Management

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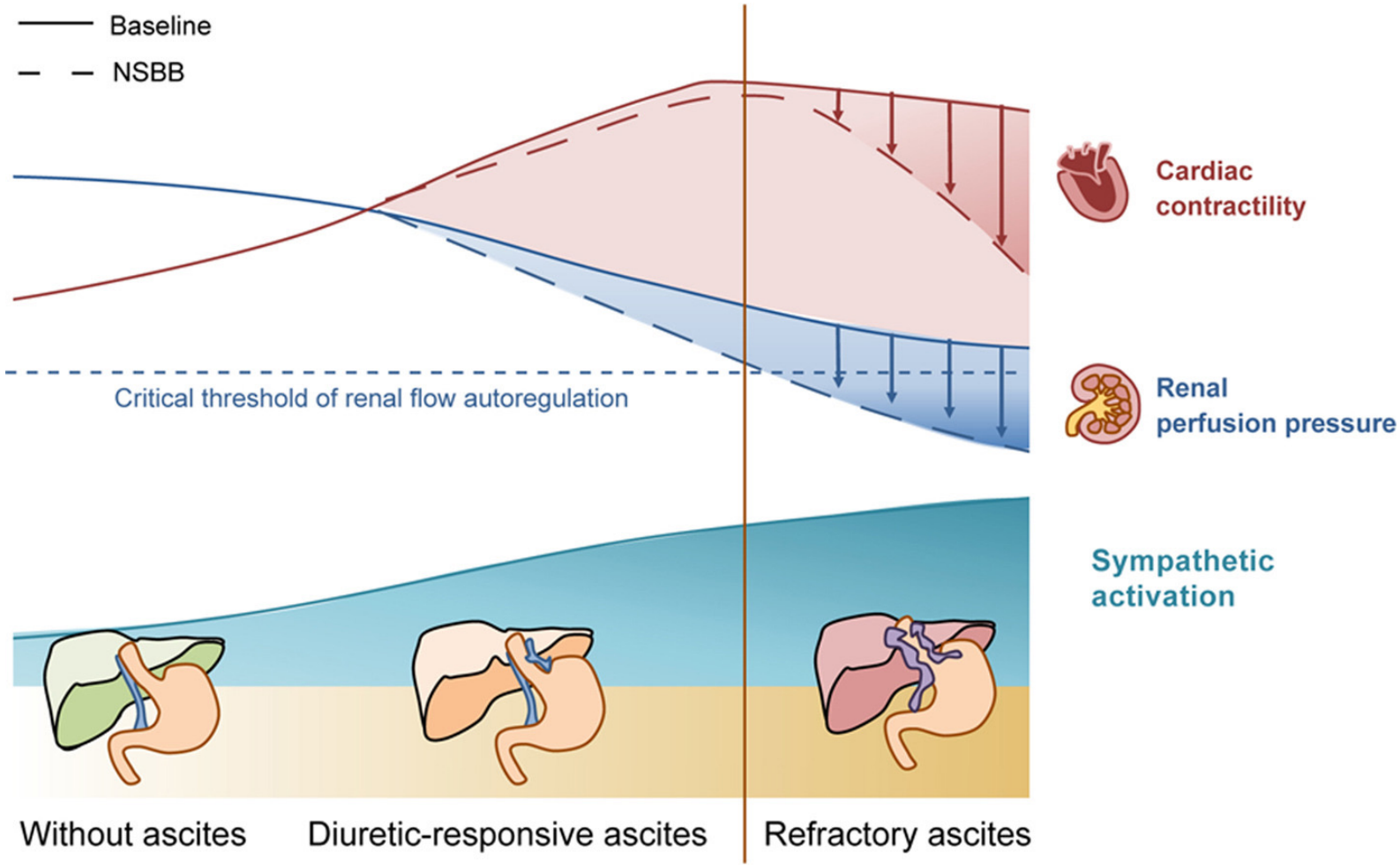
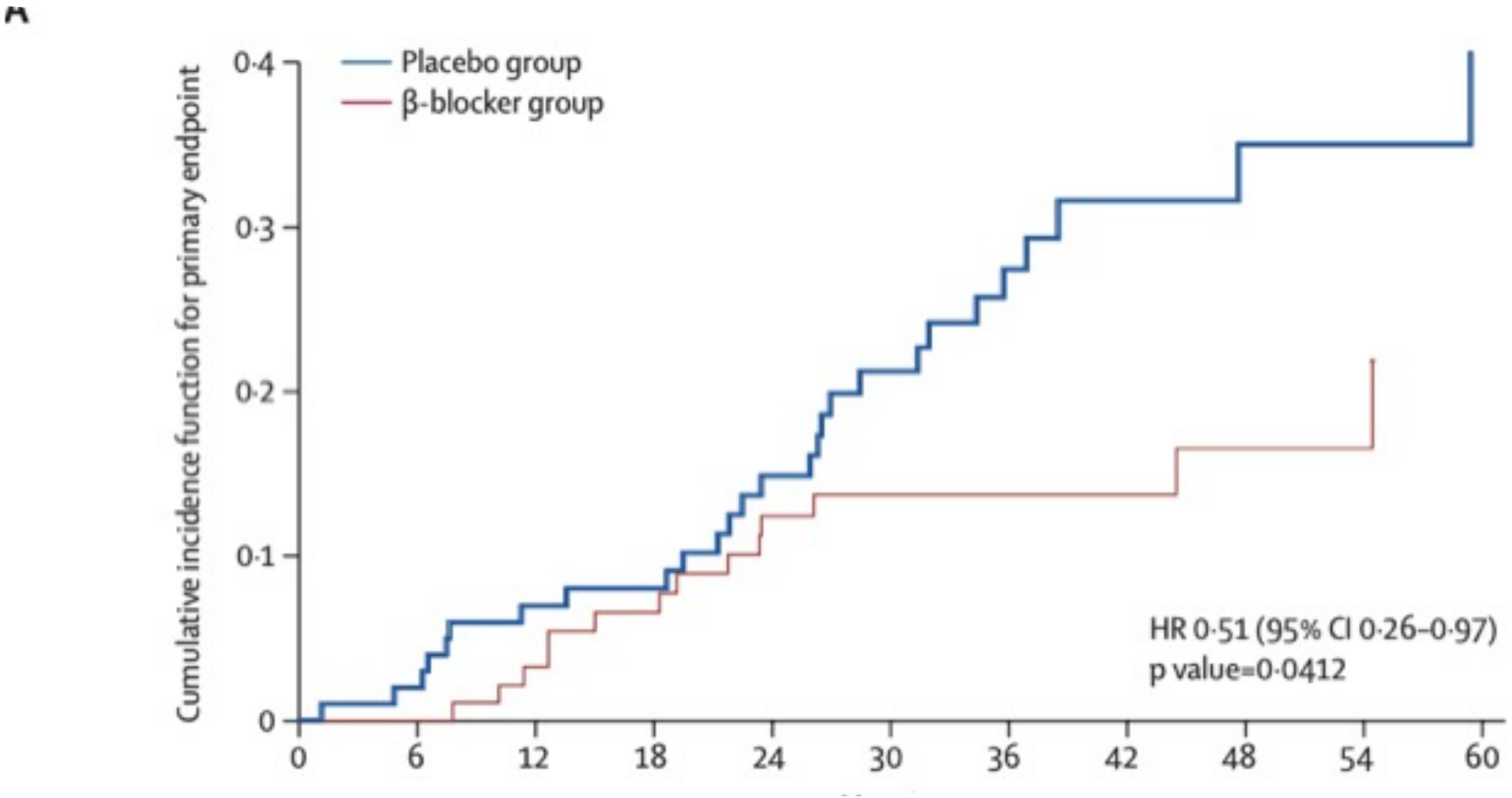
#1: Should I Stop the Beta Blocker?



Téllez, Luis, et al. "Non-selective beta-blockers impair global circulatory homeostasis and renal function in cirrhotic patients with refractory ascites." *Journal of Hepatology* 73.6 (2020): 1404-1414.



Villanueva, Càndid, et al. "β blockers to prevent decompensation of cirrhosis in patients with clinically significant portal hypertension (PREDESCI): a randomised, double-blind, placebo-controlled, multicentre trial." *The lancet* 393.10181 (2019): 1597-1608.

Should I Stop the Beta Blocker?

- **No** – Exercise caution:
  - SBP < 90 mm Hg
  - Serum Na < 130 mEq/L
  - AKI (Cr > 132 mmol/L or > 1.5 mg/dL)
- **If you do hold the beta blocker, can restart after the inciting event has resolved**

#2: Prophylaxis for SBP

- Secondary Prophylaxis after SBP
- Primary Prophylaxis after Gastrointestinal Bleeding
- Primary Prophylaxis if Total Ascitic Protein < 15 g/L + Impaired Liver / Kidney Dysfunction

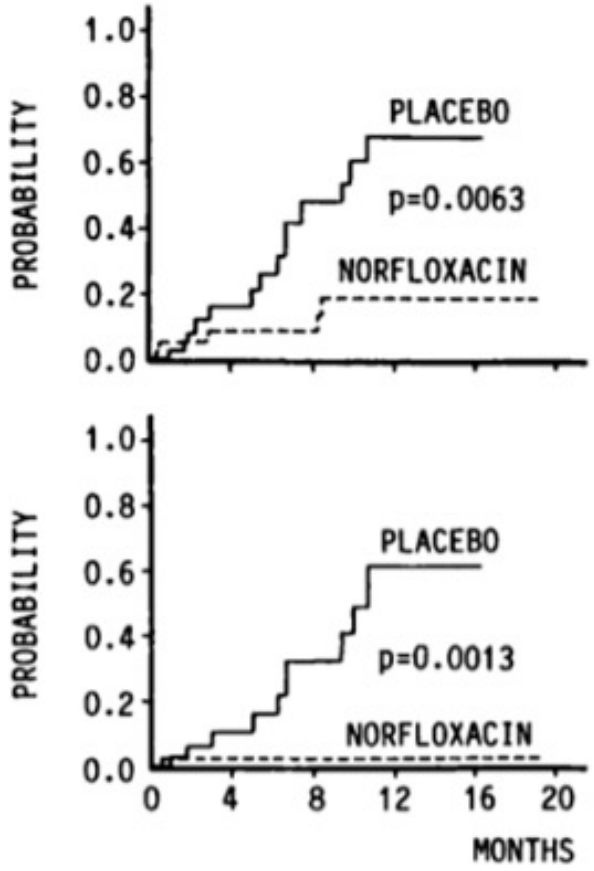
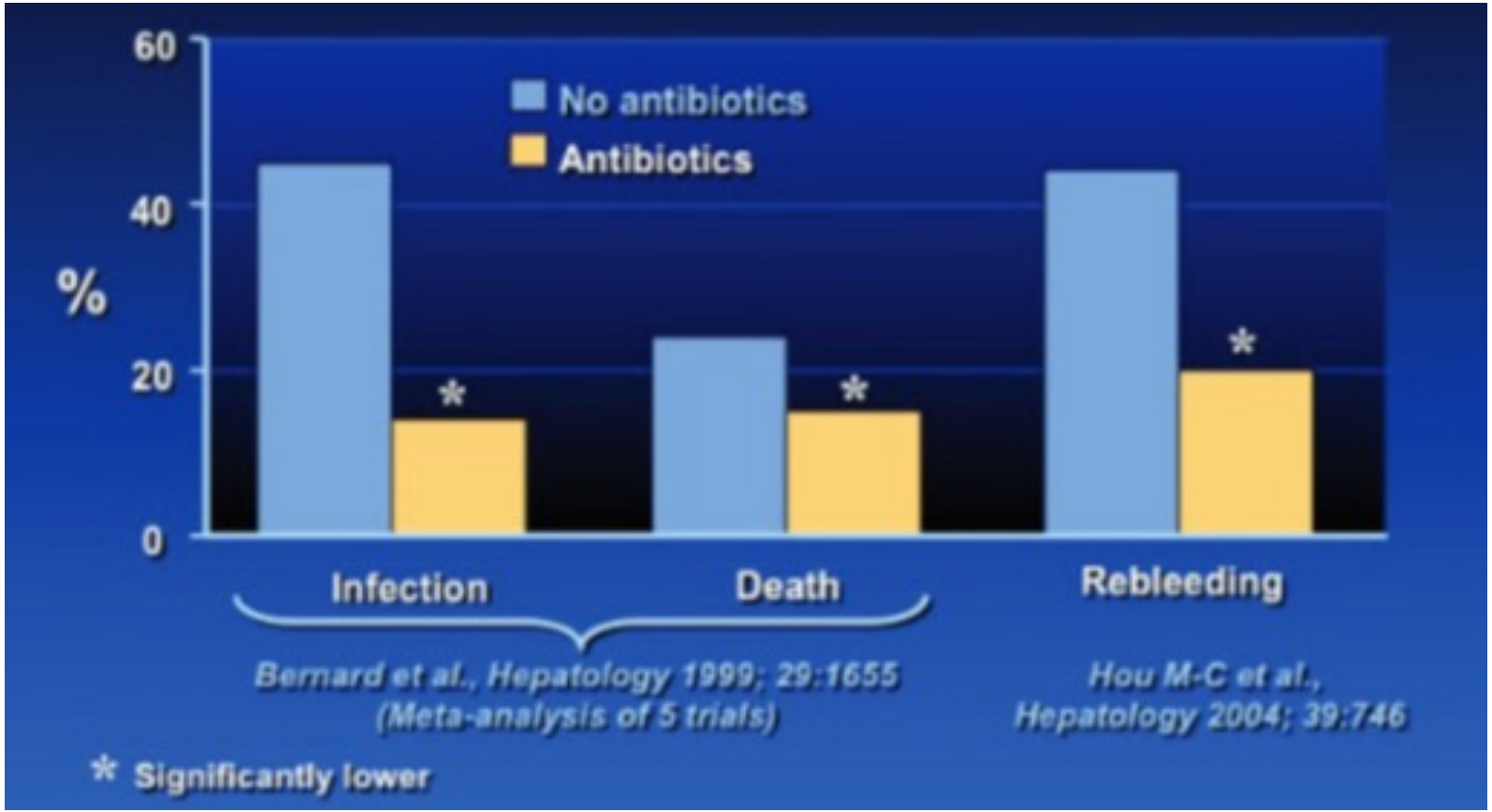


FIG. 2. Upper graph: Cumulative probability of SBP recurrence in patients from both groups. Lower graph: Cumulative probability of SBP recurrence caused by aerobic gram-negative bacilli in patients from both groups.

- **Recurrence rate ↓ from ~ 70% to 20% with norfloxacin after an episode of SBP.**

Ginés, Pere, et al. "Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial." *Hepatology* 12.4 (1990): 716-724.


60
40
20
0
%
No antibiotics
Antibiotics
*
*
*
Infection
Death
Rebleeding
Bernard et al., Hepatology 1999; 29:1655
(Meta-analysis of 5 trials)
Hou M-C et al.,
Hepatology 2004; 39:746
* Significantly lower

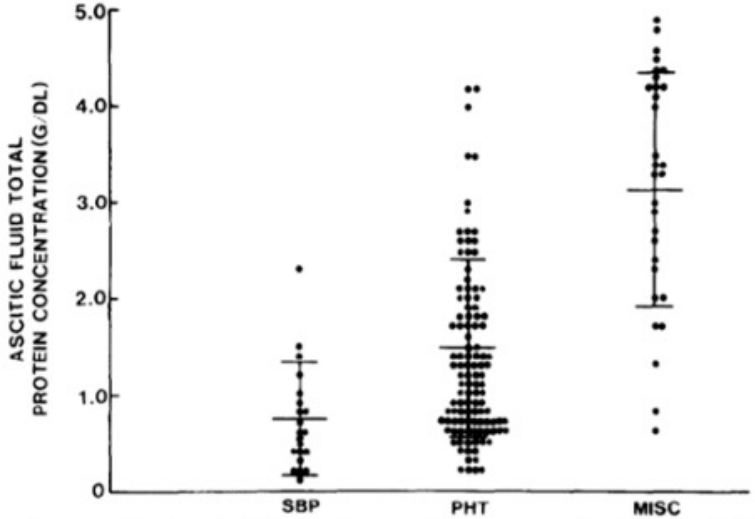
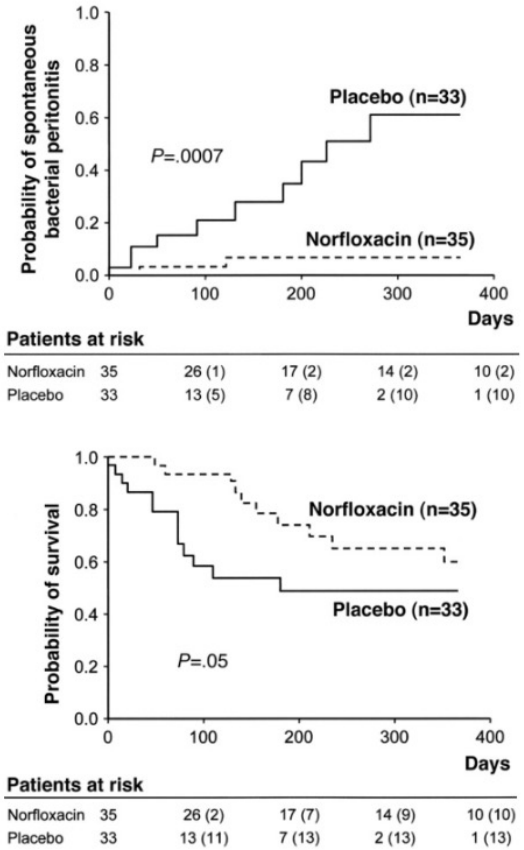


Figure 1. Total protein concentration in ascitic fluid of various types. SBP, spontaneous bacterial peritonitis; PHT, sterile portal hypertension-related; MISC, miscellaneous.



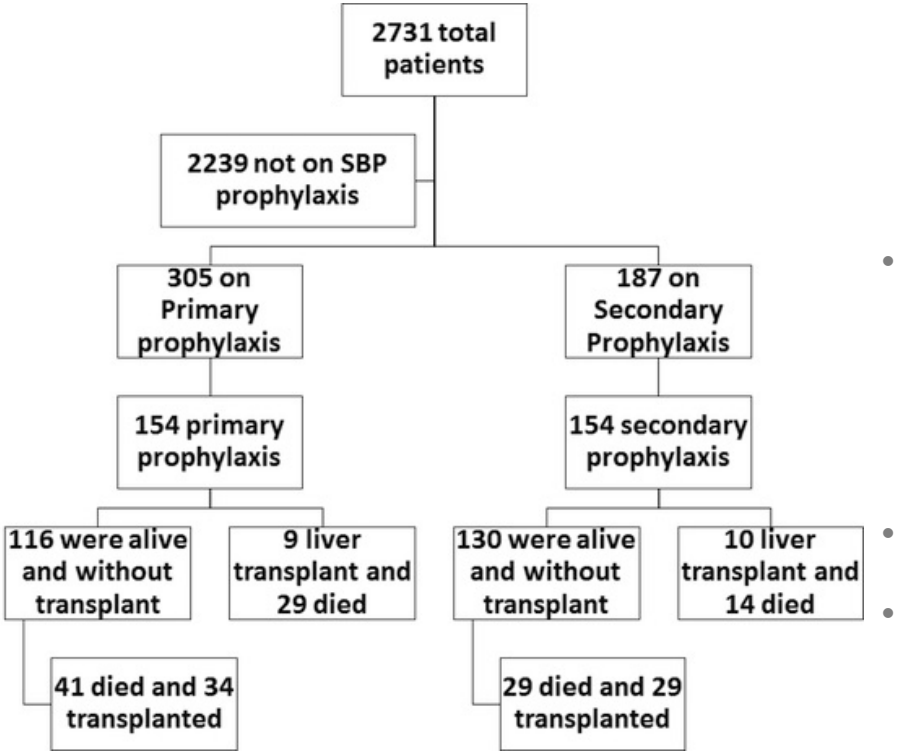
Runyon, Bruce A. "Low-protein-concentration ascitic fluid is predisposed to spontaneous bacterial peritonitis." *Gastroenterology* 91.6 (1986): 1343-1346.

Fernández, Javier, et al. "Primary prophylaxis of spontaneous bacterial peritonitis delays hepatorenal syndrome and improves survival in cirrhosis." *Gastroenterology* 133.3 (2007): 818-824.

Propensity matched on admission MELD and serum albumin

Inpatient outcomes

90 day outcomes



- ↑ SIRS, ICU admission, in-hospital mortality
- ↑ AKI
- ↑ 90-day mortality

Primary SBP prophylaxis in US Veterans System

Two Complementary Methods to Gauge the Relevance Of Primary SBP prophylaxis in Veterans

Corporate VA Data Warehouse	**Individual Site Antibiograms**	
>7500 Veterans with first SBP comparing those on vs not on primary SBP prophylaxis	across 50 states for *E. coli* & *K. pneumoniae*	

Primary SBP Prophylaxis → ↑ resistance, Second SBP & Liver transplant
Antibiograms show fluoroquinolone resistance to *E. Coli* up to 50%

Badal and Silvey, et al. *Hepatology.*

HEPATOLOGY

#2: Prophylaxis for SBP

- **Secondary Prophylaxis after SBP**
- **Primary Prophylaxis after Gastrointestinal Bleeding**
- **Primary Prophylaxis if Total Ascitic Protein < 15 g/L + Impaired Liver / Kidney Dysfunction**

Take-Home Points: New-Onset Ascites

- Perform paracentesis early (< 12 h)
- Do a full investigation with H&P, Labs and US w/ Dopplers to determine the etiology
- If associated with cirrhosis / PHTN:
  - Sodium restriction, diuretics
  - LVP + albumin for tense ascites
- Use beta blockers and antibiotics appropriately

Questions?

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