A multi-center randomized controlled study of primary prevention of esophageal variceal bleeding in cirrhotic patients treated with HVPG-guided beta-blocker therapy or standard heart rate-guided beta-blocker therapy.

Published: 01-11-2012
Last updated: 19-07-2024

To determine cost-effectiveness of hepatic venous pressure gradient (HVPG)-guided nonselective beta-blocker therapy as compared to standard heart rate-guided beta-blocker therapy in the primary prevention of esophageal variceal bleeding in cirrhotic...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal haemorrhages NEC
Study type	Interventional

Summary

ID

NL-OMON55566

Source
ToetsingOnline

Brief title
PORTHOS trial

Condition

- Gastrointestinal haemorrhages NEC
- Hepatic and hepatobiliary disorders
- Therapeutic procedures and supportive care NEC

Synonym
Esophageal variceal bleeding, esophageal variceal hemorrhage

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Betablocker therapy, Esophageal variceal bleeding, Hepatic Venous Pressure Gradient, Prevention

Outcome measures

Primary outcome

First variceal bleeding episodes occurring within the first two years.

Secondary outcome

Mortality

Occurrence of other cirrhosis-related complications

Occurrence of hepatocellular carcinoma

Costs of treatments

Adverse effects

Study description

Background summary

About 50% of cirrhotic patients who use nonselective beta-blockers (NSBB) for primary prevention of variceal bleeding do not reach target hemodynamic response, defined as HVPG < 12 mmHg or a > 10% decrease in HVPG from baseline. These so-called hemodynamic nonresponding patients have significantly higher rate of first esophageal variceal hemorrhage as compared to patients who do respond to NSBB.
Although the efficacy of HVPG monitoring in the primary prevention of variceal hemorrhage is not an issue, international institutions that publish guidelines differ in their recommendations concerning HVPG monitoring. As a result,

practice currently varies widely.
We hypothesize that HVPG-directed primary prophylaxis leads to a reduction in first variceal bleeding episodes and is cost-effective in the long term.

Study objective

To determine cost-effectiveness of hepatic venous pressure gradient (HVPG)-guided nonselective beta-blocker therapy as compared to standard heart rate-guided beta-blocker therapy in the primary prevention of esophageal variceal bleeding in cirrhotic patients.

Study design

A multi-center randomized controlled study comparing nonselective beta-blocker therapy guided by the hemodynamic response as determined by the difference in HVPG before and after starting oral nonselective beta-blockers, to standard heart rate-guided nonselective beta-blocker therapy in patients with esophageal varices due to liver cirrhosis.

Intervention

-In HVPG-group: Perform baseline HVPG measurement, then start propranonlol 20 mg orally twice daily (BID), increase the dose stepwise with 3 days interval to decrease the heart rate to maximum tolerated dose. After 4 weeks a second HVPG is performed.
In hemodynamic responders (HVPG second measurement< 12 mmHg or >10% reduction in HVPG compared to baseline) beta-blockers are continued until end of follow-up.
In hemodynamic nonresponders (who do not reach target decrease in HVPG), beta-blockers are continued and repeated endocopic band ligation is performed with 2-4 weeks interval until complete obliteration of large varices.
-In control group: Start propranolol 20 mg BID, increase the dose stepwise with 3 days interval to maximum heart rate-guided tolerated dose.

Study burden and risks

In the control group standard of care is given.
In the study arm two extra admissions in day-care setting (for 3 h) for HVPG measurements are required for the study protocol. Hepatic venous pressure gradient measurement is performed via catheterisation of the internal jugular vein. Complications due to HVPG measurement are very rare and include hemorrhage near the insertion place or cardiac arrhythmia during progression of the catheter through the heart.
In hemodynamic nonresponders from the study arm, repeated endoscopic band ligation is performed in daycare setting with intervals of 2-4 weeks.
Endoscopic band ligation is standard of care in primary prohylaxis of variceal

hemorrhage in patients who do not tolerate betablockers and is always performed as secondary prophylaxis. Complication rate of endoscopic bandligation is approximately 2%, with the most frequent complication hemorrhage from a banding ulcer or varix.
Patients will visit the outpatient clinic during dose escalation on a weekly basis until a stable dose is reached. Then a 3 monthly outpatient clinic visit including physical examination scheme will be followed. The site visits required for dose escalation and outpatient clinic follow-up are standard of care.
Patients are requested to complete biannual questionnares, and health VAS.
During the study a total of 200 cc blood will be taken in 9 sessions.

Contacts

Public
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL
Scientific
Leids Universitair Medisch Centrum

Albinusdreef 2
Leiden 2333 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Liver cirrhosis
Esophageal varices >=5 mm, no prior variceal bleeding
Patient age 18 years or older

Exclusion criteria

Contraindications to beta-blocker therapy
Pregnancy
Prior variceal hemorrhage
Esophageal varices in the absence of liver cirrhosis
Intermediate, advanced or terminal stage hepatocellular carcinoma (BCLC stage B, C or D)
Refractory ascites
Hepatorenal syndrome
Prior treatment or prophylaxis for esophageal varices or esophageal variceal bleedings (propranolol use, TIPS, endoscopic bandligation, endoscopic sclerotherapy)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-04-2013
Enrollment:	66
Type:	Actual

Ethics review

Approved WMO Date:	01-11-2012
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	22-05-2014
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	02-07-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	17-01-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT01618890
CCMO	NL40226.058.12