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REVIEW

Is carvedilol superior to propranolol in patients with cirrhosis with portal hypertension: a systematic and meta-analysis

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Abstract

Background: Carvedilol has shown greater potency than propranolol as a β-blocker in managing cardiac conditions. However, its efficacy in reducing portal hypertension (PHTN) in patients with cirrhosis remains unclear. This study evaluates the efficacy and safety of carvedilol compared with propranolol in managing PHTN.

Methods: A systematic review and meta-analysis were conducted using PubMed, Scopus and Embase databases. Randomized controlled trials comparing carvedilol and propranolol were included. Primary outcomes were changes in hepatic venous pressure gradient, wedge hepatic venous pressure and free hepatic venous pressure. Secondary outcomes included heart rate, cardiac output and mean arterial pressure. Tertiary outcomes assessed adverse event incidences.

Results: Six randomized controlled trials involving 336 patients (171 carvedilol, 165 propranolol) were analysed. Carvedilol significantly reduced hepatic venous pressure gradient (mean difference (MD): 2.22 (95% CI 1.82–2.62); $p<0.00001$) and wedge hepatic venous pressure (MD: 2.38 (95% CI 1.92–2.84); $p<0.00001$). Propranolol significantly reduced cardiac output (MD: −0.60 (95% CI −0.74 to −0.45); $p<0.00001$). Mean arterial pressure was significantly lower in the carvedilol group (MD: 1.79 (95% CI 0.38–3.20); $p=0.01$). Adverse events, such as orthostatic hypotension and increased diuretic use, were more frequent in the carvedilol group but were manageable.

Conclusion: Carvedilol demonstrates superior efficacy in reducing PHTN compared with propranolol, with a slightly higher but tolerable adverse event profile. It may be considered the first-line treatment for PHTN. Further research is needed to validate long-term benefits and safety.

Keywords: carvedilol, liver cirrhosis, non-selective β-blocker, portal hypertension, propranolol.

Citation

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Introduction

Portal hypertension (PHTN) is one of the consequences of liver cirrhosis and is responsible for its most severe complications, including ascites, variceal bleeding and encephalopathy.[1] PHTN is described as an increase in hepatic sinusoidal pressure to 6 mmHg or more, and results in the formation of portosystemic collaterals, which shunt portal blood to the systemic circulation. Many studies have suggested that a reduction in PHTN improves clinical outcomes in patients with liver cirrhosis, ascites, hepatic encephalopathy, gastrointestinal bleeding and hepatorenal syndrome as well as reducing mortality.[2–4] Since 1980, the role of non-selective β-blockers (NSBBs) has been extensively studied. NSBBs play a role in decreasing PHTN. By inhibiting the β1 and β2 receptors, NSBBs reduce cardiac output and splanchnic blood flow, resulting in splanchnic vasoconstriction caused by the unopposed effect of the α1 receptor.[5] Most studies have reported a significant reduction in variceal bleeding, portal hypertensive gastropathy and spontaneous bacterial peritonitis development following NSBB use.[6–11] Propranolol, an extensively studied β-blocker, is the drug of choice in patients with cirrhosis and PHTN. However, up to 60% of patients administered

propranolol do not achieve a reduction of the hepatic venous pressure gradient (HPVG), resulting in an increased risk of bleeding.[12–14] In patients with therapeutic failure with propranolol, carvedilol achieved a haemodynamic response rate as high as 60%.[15,16] Carvedilol is a new addition to the treatment of PHTN. As an NSBB, carvedilol decreases heart rate and cardiac output and results in splanchnic vasoconstriction, reducing portal blood inflow and pressure. In addition to β-blocker activity, carvedilol is reported to have α1 adrenergic receptor blocking activity, decreasing hepatic vascular tone and hepatic resistance and further decreasing portal pressure.[17] Frishman et al.[18] reported that carvedilol is four times more potent than propranolol in trials conducted for heart failure efficacy. Therefore, carvedilol is a potent alternative therapy to propranolol in patients with therapeutic failure. Nevertheless, the use of either carvedilol or propranolol is recommended for the primary prevention of variceal bleeding.[19] The present study evaluates the efficacy and safety profiles of carvedilol and propranolol in patients with cirrhosis and PHTN.

Methods

Literature search

An extensive literature search was performed by using PubMed, Scopus and Embase. The first phase of the search involved the terms "non-selective beta-blocker", "NSBB", "carvedilol" and "propranolol". The second phase searched for the terms "hypertension", "HTN", "portal hypertension" and "PHTN". A third phase used the terms "liver cirrhosis", "cirrhosis" and "decompensated cirrhosis" to select articles retrieved from the first and second phases. Citations were downloaded and imported to Zotero 5.0. Two independent authors (SR and PBM) screened the eligible studies, and a third author (BM) handled any disagreement regarding the inclusion and exclusion criteria (Table 1).

Inclusion and exclusion criteria

All randomized control trials (RCTs) from the last 22 years (January 2000 to June 2024) associated with an NSBB (carvedilol and propranolol) in patients with cirrhosis and PHTN, irrespective of age, sex and dose, were included. Review articles, case reports, case series, observational studies, editorials, abstracts, case-control studies and studies with insufficient data were excluded from the study.

Outcomes

The primary outcome of interest was a change in HVPG, wedge hepatic venous pressure (WHVP), free hepatic venous pressure (FHVP) and hepatic blood flow (HBF). The secondary outcomes of interest were heart rate, cardiac output, mean pulmonary artery pressure (MPAP), right arterial pressure (RAP), systemic vascular resistance (SVR), mean arterial pressure (MAP) and serum creatinine. The tertiary outcome of interest was the incidence of adverse events, including haematemesis, hypotension, increased diuretics, shortness of breath, dizziness, ascites and hepatic encephalopathy.

Study selection and data extraction

All included studies were subjected to title and abstract screening, followed by full text and supplementary data screening. Two authors (SR and PBM) independently assessed the eligible studies to determine the appropriateness for inclusion of the studies. From eligible studies, the following information was obtained in pre-designed data extraction proforma in an Excel sheet: (1) first author name, (2) year of publication, (3) study design, (4) country, (5) number of participants in case and control groups, (6) change in HPVG, WHVP, FHVP, HBF, heart rate, cardiac output, MPAP, RAP, SVR, MAP and renal function, and (7) incidence of haematemesis, hypotension, dizziness, ascites and hepatic encephalopathy.

Quality assessment

Two reviewers (SR, BM) independently evaluated each study's risk of bias and disagreement as per Cochrane Handbook of Systematic Reviews of Intervention.[20] We classified trials as having a low risk of bias if none of the domains were associated with an unclear or high risk of bias; otherwise, they were classified as having an unclear (at least one domain was assessed as having unclear risk without any high-risk domains) or high risk of bias.

Data synthesis and analysis

The meta-analysis was performed using RevMan 5.3 software amongst studies that reported similar outcomes. Continuous data were analysed as a mean difference and dichotomous data as an odds ratio. If baseline and endpoint scores were given for continuous data, we analysed the change from baseline to the endpoint and calculated the mean difference (MD) and standard error. The final pooled result was presented as MD along with the 95% CI. The I^2 statistic was used to measure heterogeneity in each included study analysis. The fixed effect model was used when the $p>0.1$ and when the I^2 value was less than 50%; otherwise, a random effect model was used. The study was performed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.[21]

Registration

This study was not registered with PROSPERO. We acknowledge the importance of such registrations and

Table 1. Study characteristics.

Reference, country	Duration	Treatment		Sample size		Inclusion criteria	Exclusion criteria	Outcomes
		Case	Control	Case (analysed)	Control (analysed)			
Hobolth et al.,[22] Denmark	12 weeks	• Carvedilol (3.125 mg OD) • Drug titration was performed weekly, aiming at a pulse reduction of 25% with a HR not below 55 bpm and SBP not below 90 mmHg • Maximum dose: 25mg OD • Mean dose: 14 ± 7 mg	• Propranolol (40 mg OD) • Drug titration was performed weekly, aiming at a pulse reduction of 25% with a HR not below 55 bpm and SBP not below 90 mmHg • Maximum dose: 320 mg OD • Mean dose: 122 ± 64 mg	18 (16)	15 (13)	Age >18 years, HVPG ≥12 mmHg, diagnosis of cirrhosis based on liver biopsy in 30% or classical, accepted clinical and biochemical criteria, and presence of portal hypertension, not on a β-blocker or calcium channel blocker	–	• A significant decrease in HVPG was observed in both groups. However, no significant difference was observed between the groups • Non-significant decrease in HR in both the groups • MAP significantly decreased in the propranolol group compared to carvedilol group • Significant decrease in cardiac outcomes in the carvedilol group compared to the propranolol group • No significant change was observed in the oxygenation parameter, including the alveolar arterial oxygen gradient • A significant decrease in renin was observed in the carvedilol group
Kim et al.,[26] Korea	6 weeks	• Carvedilol (6.25 mg OD) • Drug titration was performed aiming HR decrease by 25% from baseline or up to 55 bpm if tolerable by the patient, and SBP was >90 mmHg • Mean dose: 11.6 mg/dl (range, 6.25–12.5 mg/dl)	• Propranolol (20 mg BD) • Drug titration was performed, aiming at HR decrease by 25% from baseline or up to 55 bpm if tolerable by the patient and SBP was >90 mm Hg • Mean dose: 152.6 mg/dl (range, 40–320 mg/dl)	55 (47)	55 (43)	Age 20–70 years, cirrhosis diagnosed by liver biopsy or definite radiographic findings of liver cirrhosis, severe PHTN, HVPG >12 mmHg, oesophageal varix grade 2 or 3 affirmed by endoscopy within the past 3 months, CTP of <12; and not on NSBBs, angiotensin-converting enzyme inhibitor, nitrates or other vasoactive drugs within 1 month before entry	SBP of <90 mm Hg or baseline HR of <55/min, refractory ascites, hepatic encephalopathy, hepatorenal syndrome, PVT, HCC or other malignancy, EVL history of <3 months before enrolment, presence of severe systemic illness; history of gastric variceal haemorrhage, contraindication to β-blockers or α-blockers, serum bilirubin >10 mg/dl or serum creatinine ≥1.2 mg/dl, history of shunt operation or trans-jugular intrahepatic portosystemic shunt, insulin-dependent diabetes mellitus; pregnancy, unwilling to give informed consent	• From baseline, a significant decrease in HPVG was observed in the carvedilol group compared to the propranolol group. However, no significant difference was observed between the groups • A non-significant, higher response rate was observed in the carvedilol group compared to propranolol • Response rate was significantly higher with carvedilol amongst patients with high MELD score • Concerning adverse events, no significant difference was observed in the groups • Serious adverse events developed more frequently in the carvedilol group compared to the propranolol group

(*Continued*)

Table 1. (Continued)

Reference, country	Duration	Treatment		Sample size		Inclusion criteria	Exclusion criteria	Outcomes
		Case	Control	Case (analysed)	Control (analysed)			
Hobolth et al.,[23] Denmark	8 weeks	• Carvedilol (3.125 mg BD) • Drug titration was performed weekly, aiming at a pulse reduction of 25% with a HR not below 55 bpm and SBP not below 90 mmHg • Maximum dose: 25 mg/day • Mean dose: 14 ± 7 mg	• Propranolol (40 mg BD) • Drug titration was performed weekly, aiming at a pulse reduction of 25% with a HR not below 55 bpm and SBP not below 90 mmHg • Maximum dose: 320 mg/day • Mean dose 122 ± 64 mg	21 (21)	17 (17)	Age >18 years, HVPG >12 mmHg, diagnosis of cirrhosis based on liver biopsy in 30% or classical, accepted clinical and biochemical criteria, PHTN, not on a β-blocker or a calcium channel blocker	CTP of >12; HE > grade II; hepatorenal syndrome or serum creatinine >2.26 g/dl; contraindications to β-blockers such as atrioventricular block, insulin-dependent diabetes mellitus, asthma or chronic obstructive pulmonary disease; treatment with vasoactive drugs or blood transfusion during the a week before inclusion; malignancy or life expectancy less than 3 months	• Compared to baseline, HPVG was significantly decreased in the carvedilol group compared to the propranolol group. However, a non-significant difference was observed between the groups • A non-significant, higher number of patients on carvedilol reported having HVPG of <12 mmHg after 90 days compared to the propranolol group • No significant effect of carvedilol was observed on HBF. However, a non-significant decrease in HBF was observed in patients with propranolol • MAP significantly decreased in the propranolol group compared to the carvedilol group • Shortness of breath and increase in diuretics were more frequent in the carvedilol group compared to the propranolol group
Gupta et al.,[24] India	4 weeks	• Carvedilol (3.125 mg BD) • Drug titration was performed, aiming at HR of 55–60 bpm • Median dose: 6.25 mg/day (6.25–12.5 mg)	• Propranolol (40 mg OD) • Drug titration was performed, aiming at HR of 55–60 bpm • Median dose: 40 mg/day (40–80 mg)	30 (29)	29 (28)	Age 18–70 years, willing to undergo HVPG measurements as per the protocol and willing to give informed consent for participation in the study	Refusal to provide consent to participate in the study; previous medical, surgical or endoscopic treatment for PHTN; neoplastic disease of any site; splenic or PVT; pregnancy; contraindication to β-blockers; atrioventricular block; sinus bradycardia with HR of 50 bpm; arterial hypotension with SBP of <90 mmHg; heart failure; asthma; peripheral arterial disease or diabetes needing insulin treatment; renal failure; bleeding source other than oesophageal varix	• At 1 month, no significant difference was observed in HPVG and MAP in the groups • In percentage change, MAP decreased substantially in the carvedilol group compared to the propranolol group • In terms of stratified HVPG respondents and non-respondents, the carvedilol group showed a significant number of respondents • No significant adverse events were reported in the groups. However, the propranolol group had more adverse events (hypotension, increase in diuretics, breathing difficulty) compared to the carvedilol group

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Reference, country	Duration	Treatment		Sample size		Inclusion criteria	Exclusion criteria	Outcomes
		Case	Control	Case (analysed)	Control (analysed)			
Bañares et al.,[27] Spain	Mean of 11.1 ± 4.1 weeks	• Carvedilol (6.25 mg OD) • The dosage of both drugs was stepwise increased every 4 days until the HR was reduced by 25% or to less than 55 bpm whilst SBP was greater than 85 mmHg • Mean dose: 31 ± 4 mg/d (range, 12.5–50 mg/d)	• Propranolol (10 mg BD) • The dosage of both drugs was stepwise increased every 4 days until the HR was reduced by *25%* or to less than 55 bpm whilst SBP was greater than 85 mmHg • Mean dose: 73 ± 10 mg/d (range, 10–160)	26 (24)	25 (22)	Presence of endoscopically proven oesophageal varices without previous haemorrhage; HVPG >12 mmHg; diagnosis of cirrhosis was based on liver biopsy specimens or on clinical, biochemical or ultrasonographic findings	Age <18 or >75 years, severe liver failure evaluated by the presence of a serum bilirubin level greater than 5 mg/dL, and/or an international normalized ratio greater than 2.5 or uncontrolled HE, contraindications to P-blockers; asthma or chronic obstructive lung diseases; atrioventricular block; HR <50 bpm; peripheral arterial disease; insulin-dependent diabetes mellitus; active alcoholism; serum creatinine >2 mg/dL; HCC; refusal to participate in the study	• Carvedilol and propranolol groups showed a significant reduction in HVPG. However, carvedilol showed a more pronounced decrease in HPVG compared to propranolol • Compared to propranolol, the response rate was significantly higher in the carvedilol group • In patients with CTP scores B and C, carvedilol showed a more significant decrease in HPVG compared to the propranolol group • The carvedilol group showed a significant decrease in azygos blood flow • The propranolol group showed a significant decrease in HBF. However, carvedilol did not significantly change HBF • The propranolol group showed a significant decrease in HR and cardiac outcomes compared to the carvedilol group • The carvedilol group showed a significant increase in body weight and plasma volume with a reduction in parasympathetic nervous system activity. However, the propranolol group showed no change in either • No significant change in glomerular filtration rate was noticed in either group • Mild effects occur more frequently in the carvedilol group compared to the propranolol group • Shortness of breath and orthostatic hypotension was more in the carvedilol group compared to the propranolol group

(*Continued*)

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Table 1. (Continued)

Reference, country	Duration	Treatment		Sample size		Inclusion criteria	Exclusion criteria	Outcomes
		Case	Control	Case (analysed)	Control (analysed)			
De et al.,[25] India	1 week	Carvedilol (25 mg on day 1, followed by 6.25 mg BD)	Propranolol (80 mg on day 1 followed by 40 mg BD)	18 (18)	18 (18)	Cirrhotic with oesophageal varices; patients who had either never bled or who had experienced only one episode of variceal bleeding 7–10 days before inclusion were included	Patients with bronchial asthma, diabetes mellitus, cardiac diseases or renal disease; age <15 years; patients treated by endoscopic sclerotherapy, EVL, shunt surgeries, β or α1 adrenergic blockers, diuretics, or nitrates	• Carvedilol and propranolol showed a significant decrease in HPVG. However, carvedilol showed more pronounced results • At 90 minutes, the decrease in HPVG by carvedilol was not significantly more than that of propranolol • Both carvedilol and propranolol reduce RAP and MPAP. However, propranolol showed more pronounced results compared to carvedilol • The response rate was higher in patients with carvedilol • The study reported no significant difference in either drug concerning the response of alcoholic and non-alcoholic cirrhotic

BD, twice a day; bpm, beats per minute; CTP, Child-Turcotte-Pugh; EVL, endoscopic variceal ligation; HBF, hepatic blood flow; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; HR, heart rate; HVPG, hepatic venous pressure gradient; MAP, mean arterial pressure; MPAP, mean pulmonary artery pressure; NSBB, non-selective β-blocker; OD, once a day; PHTN, portal hypertension; PVT, portal vein thrombosis; RAP, right arterial pressure; SBP, systolic blood pressure.

commit to registering future systematic reviews and meta-analyses with PROSPERO to enhance transparency and rigour.

Results

Search result and included studies

The initial search yielded 7820 records (PubMed: 1498; Scopus: 2937, and Embase: 3385). After title and duplicate screening, 5853 records were analysed. Out of 5853, 5844 did not meet the inclusion criteria. Of these, nine articles were considered for the full review. Out of nine, six studies met the inclusion criteria and were included in the systematic review and meta-analysis (Figure 1).

Study characteristics

All included studies were RCTs. Out of six, two studies were from Denmark,[22,23] two from India[24,25] and one each from Korea[26] and Spain.[27] All included studies administered carvedilol or propranolol to the included participants. Collectively, studies presented the data for 336 patients with cirrhosis (carvedilol: 171 and propranolol: 165) with PHTN. All included studies measured HPVG, WHVP, FHVP, HBF, heart rate, cardiac output, MPAP, RAP, SVR, MAP and renal function (Table 1).

Risk of bias and quality assessment

All included studies define the evaluation and inclusion–exclusion criteria before participant enrolment. All selected studies performed the same diagnostic test on

Figure 1. PRISMA flow diagram.[21]

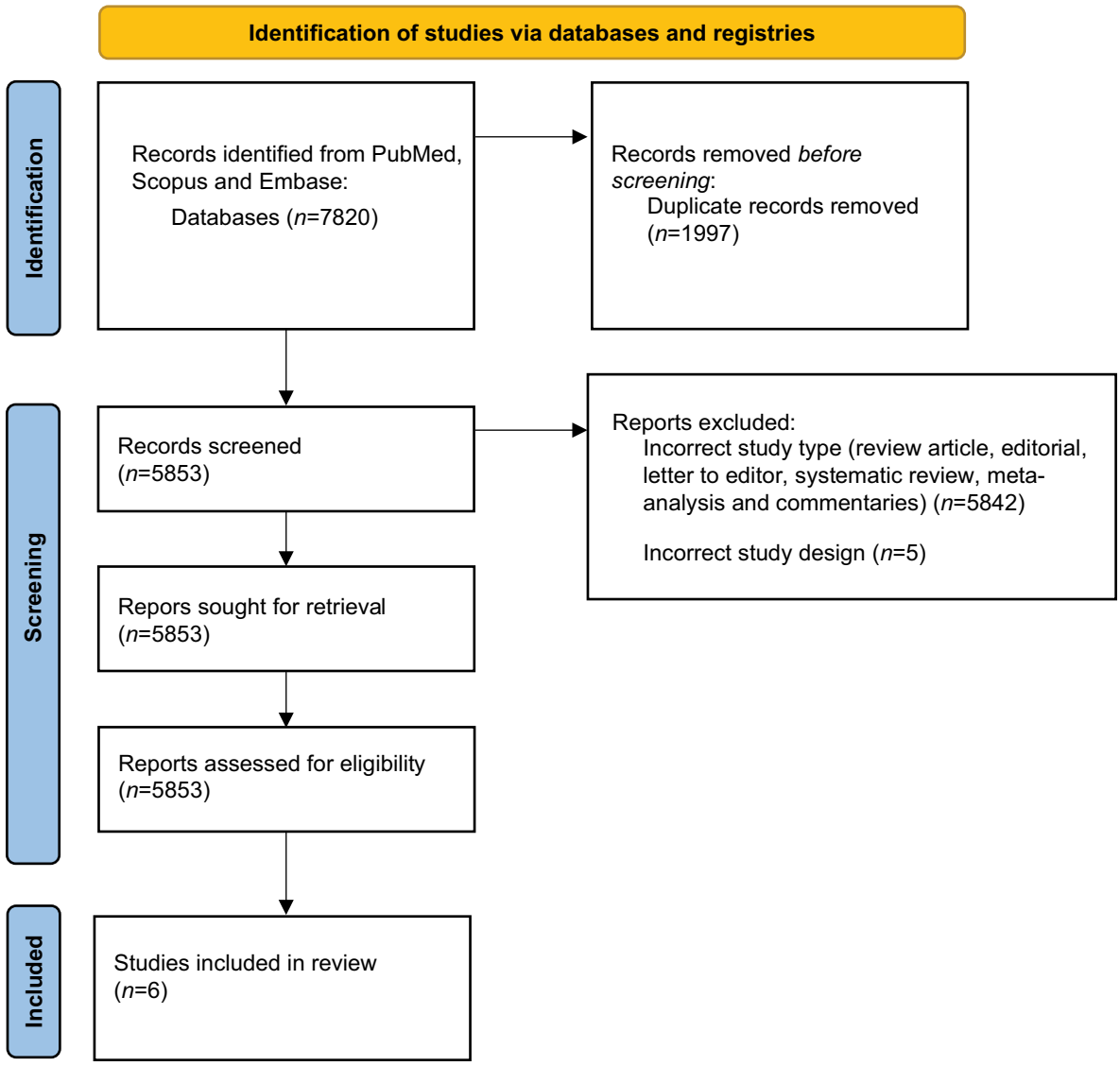
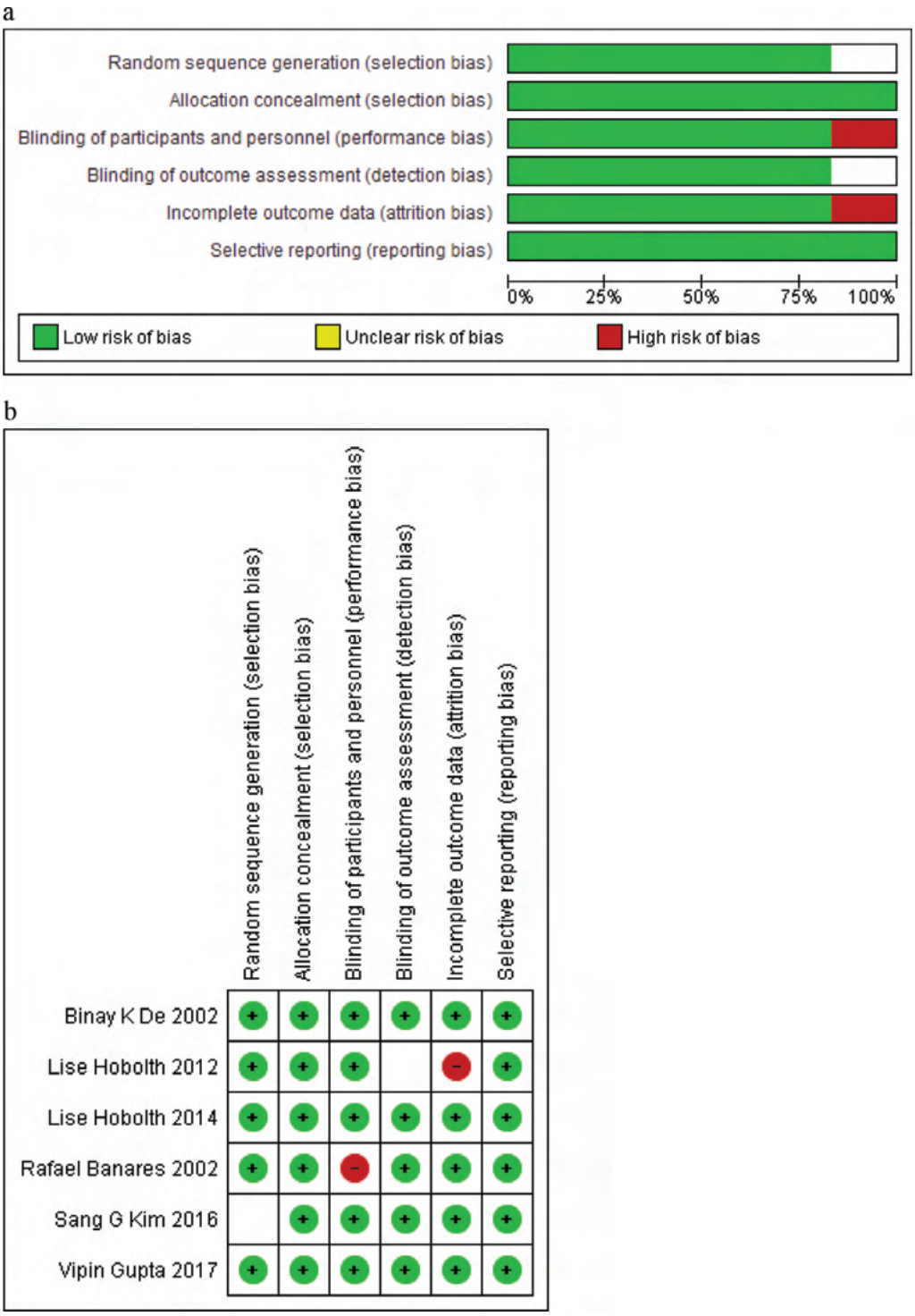


Figure 2. Risk of bias graph (a) and summary (b).



Data taken from Refs.[22–27]

both case and control groups over a similar time frame. No study was excluded on the risk of bias assessment (Figure 2).

Primary outcomes

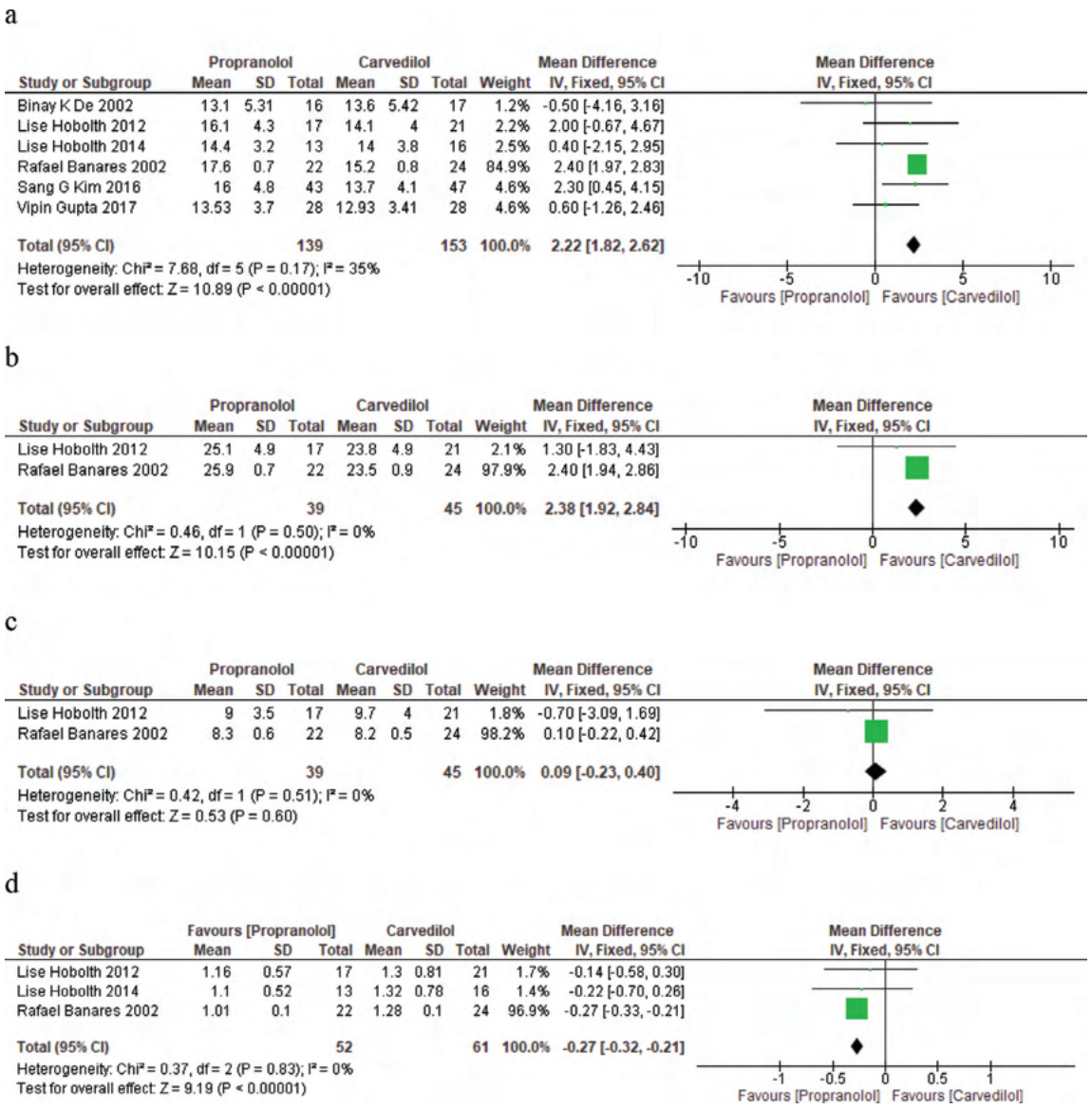
Hepatic venous pressure gradient

In the meta-analysis of six studies,[22–27] HVPG was significantly low in the carvedilol group compared with the propranolol group (MD 2.22 (95% CI 1.82–2.62); $p<0.00001$; I^2: 35%) (Figure 3a).

Wedge hepatic venous pressure

In the meta-analysis of two studies,[23,27] WHVP was significantly lower in the carvedilol group than in the propranolol group (MD 2.38 (95% CI 1.92–2.84); $p<0.00001$; I^2: 0%) (Figure 3b).

Figure 3. Primary outcomes: hepatic venous pressure gradient (a), wedge hepatic venous pressure (b), free hepatic venous pressure (c) and hepatic blood flow (d).



Data taken from Refs.[22–27]

Free hepatic venous pressure

In the meta-analysis of two studies,[23,27] when compared, no significant difference was observed in FHVP value between the carvedilol and propranolol groups (MD 0.09 (95% CI −0.23 to 0.40); p=0.60; I^2: 0%) (Figure 3c).

Hepatic blood flow

In the meta-analysis of three studies,[22,23,27] HBF was significantly higher in the carvedilol group than in the propranolol group (MD −0.27 (95% CI −0.32 to −0.21); p<0.00001; I^2: 0%) (Figure 3d).

Secondary outcomes

Heart rate

In the meta-analysis of five studies,[22–25,27] heart rate was non-significantly lower in the propranolol group than in the carvedilol group (MD −3.29 (95% CI −8.52 to 1.94); p=0.22; I^2: 95%) (Figure 4a).

Cardiac output

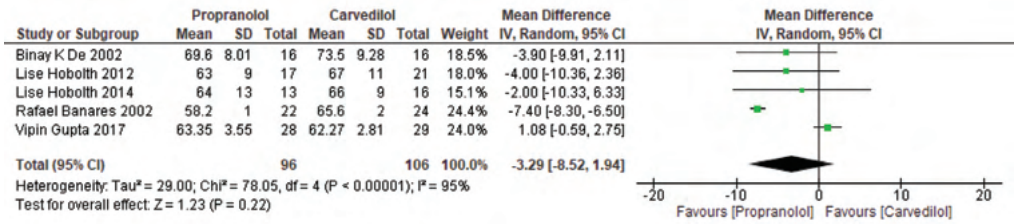
In the meta-analysis of two studies,[22,27] cardiac output was significantly lower in the propranolol group than in the carvedilol group (MD −0.60 (95% CI −0.74 to −0.45); p<0.00001; I^2: 0%) (Figure 4b).

Mean pulmonary artery pressure

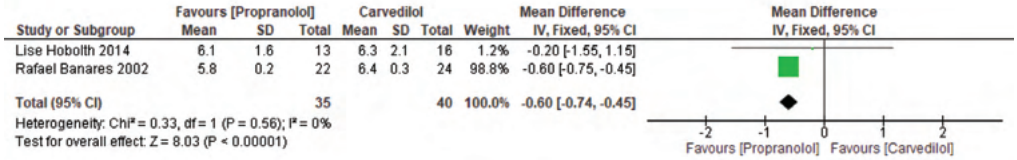
In the meta-analysis of two studies,[25,27] MPAP was significantly lower in the carvedilol group than in the propranolol group (MD 3.11 (95% CI 2.37–3.86); p<0.00001; I^2: 0%) (Figure 4c).

Figure 4. Secondary outcomes: heart rate (a), cardiac output (b), mean pulmonary artery pressure (c), right arterial pressure (d), systemic vascular resistance (e), mean arterial pressure (f) and serum creatinine (g).

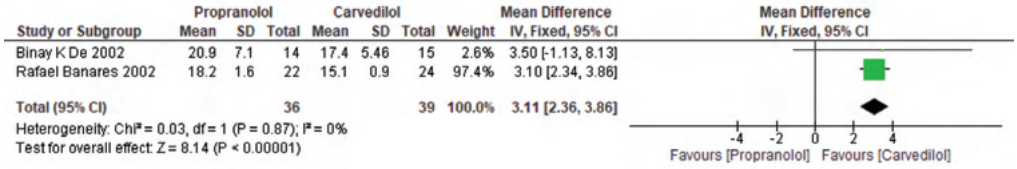
a



b



c



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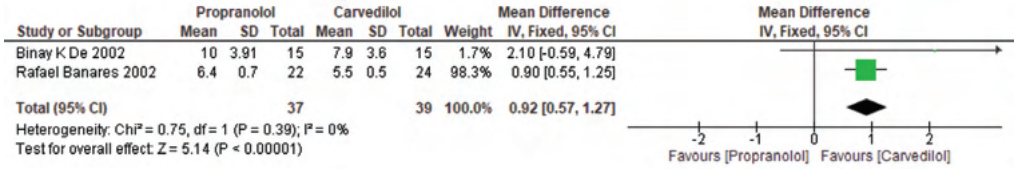

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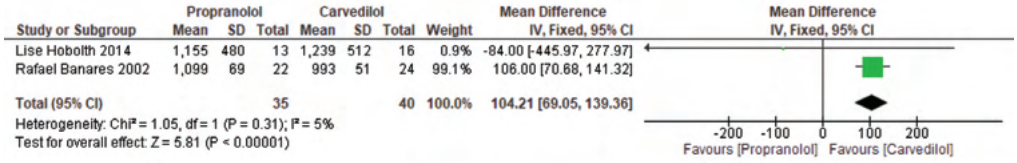

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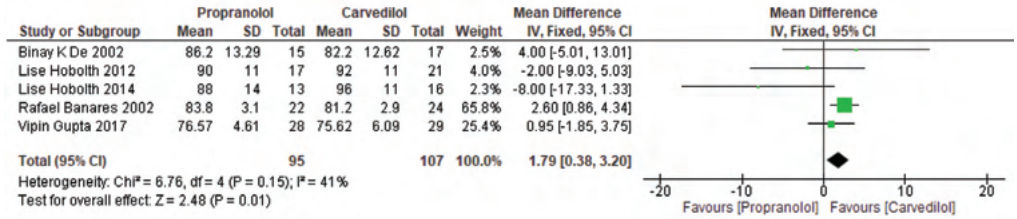

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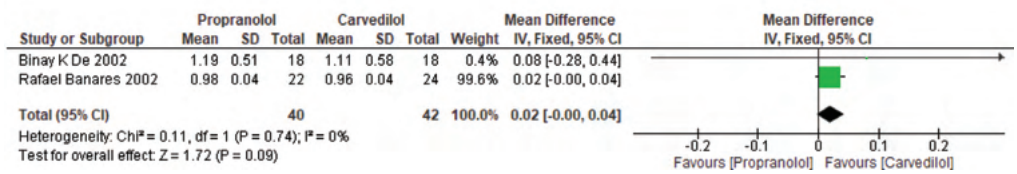


Data taken from Refs.[22–25,27]

Right arterial pressure

In the meta-analysis of two studies,[25,27] RAP was significantly lower in the carvedilol group than in the propranolol group (MD 0.92 (95% CI 0.57–1.28); $p<0.00001$; I^2: 0%) (Figure 4d).

Systemic vascular resistance

In the meta-analysis of two studies,[22,27] SVR was significantly lower in the carvedilol group than in the propranolol group (MD 104.21 (95% CI 69.05–139.36); $p<0.00001$; I^2: 5%) (Figure 4e).

Mean arterial pressure

In the meta-analysis of five studies,[22–25,27] MAP was significantly lower in the carvedilol group than in the propranolol group (MD 1.79 (95% CI 0.38–3.20); $p=0.01$; I^2: 41%) (Figure 4f).

Renal function (serum creatinine)

In the meta-analysis of two studies,[25,27] the carvedilol group had no significant difference in renal function compared with the propranolol group (MD 0.02 (95% CI −0.00 to 0.04); $p=0.09$; I^2: 0%) (Figure 4g).

Tertiary outcomes

Incidence of haematemesis

In the meta-analysis of three studies,[23,24,26] the incidence of haematemesis was similar in both the carvedilol and propranolol groups (MD 1.12 (95% CI 0.23–5.37); $p=0.89$; I^2: 0%) (Figure 5a).

Incidence of orthostatic hypotension

In the meta-analysis of two studies,[23,27] incidence of orthostatic hypotension was non-significantly higher in the carvedilol group than in the propranolol group (MD 0.79 (95% CI 0.38–1.64); $p=0.53$; I^2: 0%) (Figure 5b).

Incidence of dizziness

In the meta-analysis of two studies,[23,26] the incidence of dizziness was non-significantly higher in the propranolol group than in the carvedilol group (MD 1.80 (95% CI 0.73–4.45); $p=0.21$; I^2: 0%) (Figure 5c).

Incidence of breathlessness

In the meta-analysis of three studies,[23,26] the incidence of breathlessness was similar in the carvedilol and propranolol groups (MD 1.07 (95% CI 0.45–2.59); $p=0.87$; I^2: 0%) (Figure 5d).

Incidence of hepatic encephalopathy

In the meta-analysis of three studies,[24,26,27] the incidence of hepatic encephalopathy was non-significantly higher in the carvedilol group than in the propranolol group (MD 0.88 (95% CI 0.27–2.82); $p=0.82$; I^2: 29%) (Figure 5e).

Incidence of increase in diuretics

In the meta-analysis of three studies,[24,26,27] a non-significant increase in diuretics use was observed in the carvedilol group compared to the propranolol group (MD 0.75 (95% CI 0.39–1.44); $p=0.38$; I^2: 31%) (Figure 5f).

Discussion

This systematic review and meta-analysis demonstrated the possible role of β-blockers in patients with liver cirrhosis with PHTN. The six identified studies were RCTs with a substantive intervention of carvedilol (n=171) and propranolol (n=165). The availability of NSBBs was proven to lead to a decrease in PHTN.

A thorough assessment of the available literature on the efficacy of carvedilol *versus* propranolol for PHTN with cirrhosis revealed a significant decrease in PHTN with carvedilol compared with propranolol treatment. In the present study, a greater number of patients with cirrhosis showed significantly lower HVPG and WHVP after carvedilol administration than after propranolol. Other studies by Razon-Gonzalez et al.[28] and Sinagra et al.[29] compared the efficacy of carvedilol and propranolol and reported that carvedilol is superior to propranolol in reducing HVPG. A clinical trial reported by Guo et al.[30] showed a significant reduction in HVPG in the carvedilol group compared with the propranolol group. However, no significant difference was observed between the carvedilol and propranolol groups concerning haemodynamic response. Aguilar-Olivos et al.[31] performed a meta-analysis to assess the efficacy of carvedilol and propranolol, reporting a significant reduction in WHVP with carvedilol, which is related to the present findings.

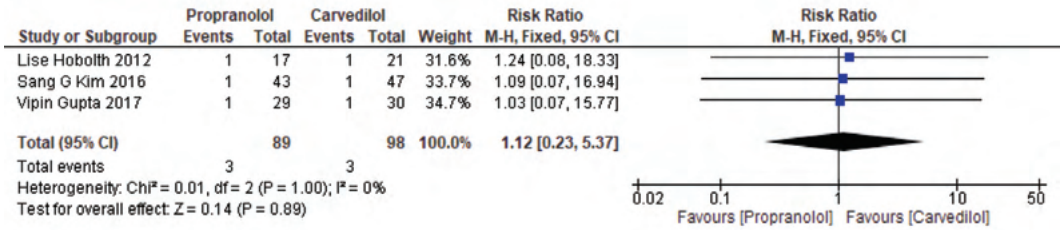
In the present study, compared with propranolol, carvedilol showed no significant difference in FHVP. Similar findings were reported by Aguilar-Olivos et al.[31] and Guo et al.[30] In addition, Guo et al.[30] reported that patients administered propranolol reported a significantly higher incidence of variceal bleeding when compared with those in the carvedilol group.

A meta-analysis of four RCTs by Aguilar-Olivos et al.[31] showed no significant difference in HBF amongst patients with liver cirrhosis on NSBB. However, the present study showed a substantial decrease in HBF in the propranolol group compared to the carvedilol group.

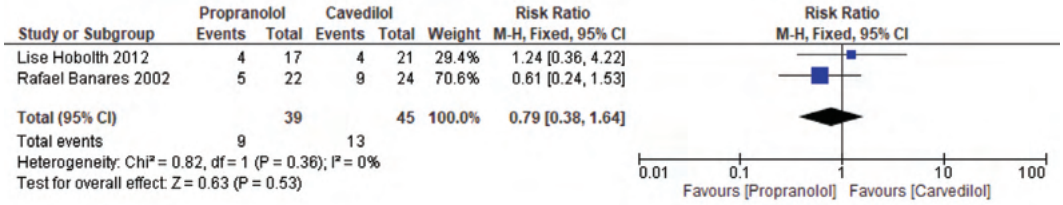
The secondary outcomes of the present study were related to the assessment of the effect of NSBBs on heart rate, MPAP, cardiac output, SVR, RAP, MAP and renal function (serum creatinine). The present study reported a non-significant and significant decrease in heart rate

Figure 5. Tertiary outcomes: incidence of hematemesis (a), orthostatic hypotension (b), dizziness (c), breathlessness (d), hepatic encephalopathy (e) and increase in diuretics (f).

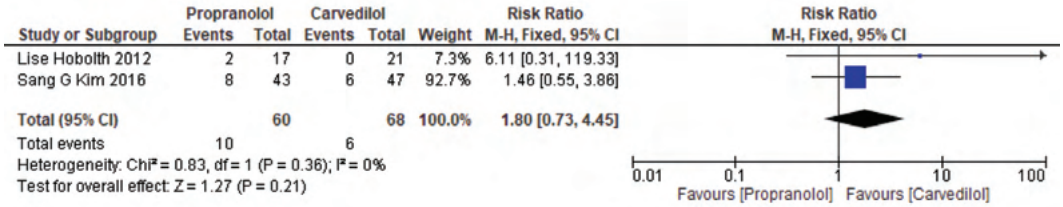
a



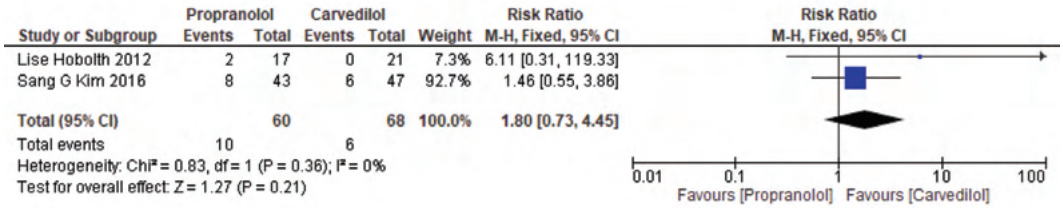
b



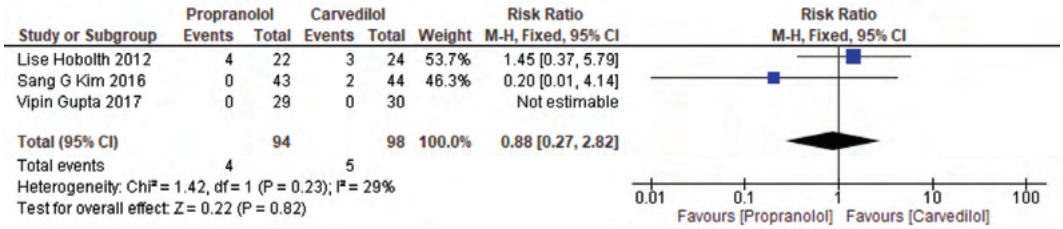
c



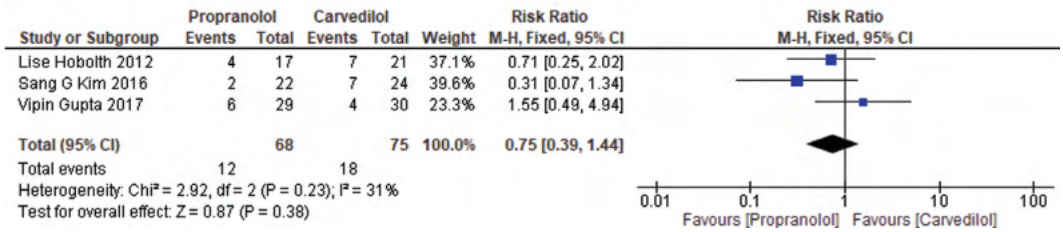
d



e



f



Data taken from Refs.[22–24,26,27]

and cardiac output in the propranolol and carvedilol groups, respectively. However, MPAP, RAP, SVR and MAP were significantly lower in the carvedilol group compared with the propranolol group. De et al.[25] performed an RCT to evaluate the efficacy of propranolol *versus* carvedilol and showed a significant reduction in heart rate. Razon-Gonzalez et al.[28] performed a meta-analysis reporting a significant decrease in HVPG and MAP in the carvedilol group compared with the propranolol group. However, a study by Ferrarese et al.[32] showed no substantial change in SVR in patients administered NSBBs.

The present study reported the increased need for diuretics in the carvedilol group. Similar results were reported by Sinagra et al.,[29] who showed an increase in the administration of diuretics in patients with carvedilol compared with patients on propranolol. A study by Rodrigues et al.[33] reported no increase in the development of new ascites in the carvedilol and propranolol groups. However, Bañares et al.[27] showed an increase in plasma volume and body weight amongst patients administered carvedilol compared with the propranolol group.

Conclusion

The present meta-analysis showed the clinical benefit of carvedilol over propranolol in managing PHTN amongst patients with liver cirrhosis. Carvedilol significantly reduced HVPG and WHVP. Even though carvedilol is reported to have non-significant, more frequent adverse events compared with propanol, carvedilol can be considered the first line of treatment for patients with cirrhosis and PHTN.

In clinical practice, the findings of the present meta-analysis showed a benefit of carvedilol for patients with cirrhosis and PHTN. Available data suggest that carvedilol may be considered for PHTN, and we did not find significant differences between carvedilol and propranolol concerning adverse events. Further future studies are needed with more patients and long-term monitoring directed at clinical outcomes, side-effects and mortality.

Study limitations

The following limitations need to be considered when assessing the above findings. (1) The study included only 336 patients, with 171 on carvedilol and 165 on propranolol. This small sample size limits the statistical power and generalizability of the results. (2) Variability in drug dosages, treatment durations and patient populations across studies may have influenced the consistency of findings, particularly in secondary outcomes. (3) The included studies were predominantly short-term, with durations ranging from 1 to 12 weeks. This restricts insights into long-term outcomes such as mortality, prevention of variceal bleeding or disease progression. (4) Whilst carvedilol demonstrated superior efficacy, its higher incidence of orthostatic hypotension and increased diuretic use raises concerns about tolerability.

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