Table 1: Evaluation of studies using the critical appraisals skills programme (CASP) toolkit[11–15]

Study	**Nagaoki *et al.* (2018)** Efficacy and safety of edoxaban for treatment of PVT following danaparoid sodium in patients with liver cirrhosis	**Naymagon *et al.* (2020)** The efficacy and safety of direct oral anticoagulants in noncirrhotic PVT	**Hanafy *et al.* (2019)** Randomised controlled trial of rivaroxaban versus warfarin in the management of acute non-neoplastic PVT	**Ai *et al.* (2020)** Efficacy and safety study of DOACs for the treatment of chronic PVT in patients with liver cirrhosis
Study type	Retrospective cohort	Retrospective cohort	Randomised controlled, open label	Prospective cohort
Clearly defined question?	Yes. Study examined the efficacy and safety of edoxaban in patients with cirrhosis and PVT following two-week treatment with danaparoid	Yes. Study examined efficacy of DOACs in non-cirrhotic PVT in comparison to standard therapies	Yes. Study examined the efficacy and safety of rivaroxaban to warfarin in HCV patients who have compensated cirrhosis	Yes. Study examined the efficacy and safety of DOACs for the treatment of chronic PVT in cirrhotic patients
Number of patients	50	330	80	80
Type of patient	Cirrhotic patients Child-Pugh A (n=29) 15 in edoxaban arm Child-Pugh B (n=16) 5 in edoxaban arm Child-Pugh C (n=5), all 5 in control arm	Non-cirrhotic patients Child-Pugh A–C excluded	Patients with hepatitis C-related compensated cirrhosis Child-Pugh A and B included Child-Pugh C excluded.	Chronic cirrhotic patients Child-Pugh A included Child-Pugh B and C excluded in rivaroxaban arm. These patients received dabigatran. Excluded patients aged over 75 years Acute PVT excluded
Well defined study population?	Not well defined. Child-Pugh C included in control arm, this could result in misleading data when presenting edoxaban arm. Detailed inclusion and exclusion criteria not mentioned.	Yes – exclusion criteria well defined. Baseline characteristics of all patients described and presented in table.	Yes – clear mention of inclusion and exclusion criteria. All patients were diagnosed with PVT <1 week before treatment. Size or extent of PVT in patients not described.	Yes – well defined, PVT diagnosed with ultrasound and CT portal venography. Propensity score matching method used for baseline consistency within groups.
Well defined Intervention?	Yes Patients initially treated with danaparoid sodium for two weeks. Treatment then switched to either edoxaban (n=20) or warfarin (n=30) for six months. Edoxaban dose was 60mg once daily or 30mg once daily (if body weight ≤ 60kg, creatinine clearance 30–50mL/min or if taking concomitant strong P-glycoprotein inhibitor to minimise bleed risk). Warfarin dose was adjusted to INR control between 1.5–2.0).	No Doses of DOACs or standard therapies not described. The mean time to initiation of therapy was 3.1 days following a diagnosis.	Yes Treated with enoxaparin 1mg/kg every 12 hours S/C for 3 days. Then switched to either rivaroxaban 10mg every 12 hours or warfarin (adjusted to INR control between 2.0–2.5) for total of six months.	Yes DOACs group (n=40), of which: Rivaroxaban 20mg once daily (n=26) Dabigatran 150mg twice daily (n=14) Control group – no anticoagulation (n=40).
Measure	Size of the PVT before treatment, at two weeks and then one, three and six months.	Complete radiographic resolution of PVT compared across anticoagulants established on follow-up imaging at least three months. Point of measure is not clearly defined and may have varied across individuals. Patients not followed up before three months were not included in analysis.	Resolution of PVT and complete recanalisation of portal vein.	Portal flow velocity is measured at 0, three and six months. CT was used to evaluate the changes in PVT: • Complete recanalisation; • Partial recanalisation; • PVT is stable or in progressive state.
Statistics	Categorical variables analysed using the X^2 test. Mann-Whitney U-test used to assess factors that influence size of PVT reduction rate. All P-values are two-tailed and P=<0.05 considered statistically significant.	Continuous patient, disease and treatment-related variables were presented by the median and interquartile range, whereas categorical variables were summarised by n (%). The Kaplan-Meier method was used to estimate the median times to event for the outcomes of complete radiographic resolution.	Categorical variables analysed using the X^2 test. Continuous variables are analysed using Student's t-test. Kaplan-Meier survival curves used to evaluate survival rate. These showed patients who were treated early with rivaroxaban showed better survival than those with warfarin. P=<0.05 considered statistically significant.	Quantitative variables are expressed as the mean ± SD, categorical variables were analysed using the X^2 tests. Comparisons between groups of quantitative variables were assessed using Student's t-test. All P-values are two-tailed and P=<0.05 considered statistically significant.
Funding/ sponsorship?	None declared. No conflict of interested declared.	None declared. No conflict of interested declared.	Research is self-funded, and no conflict of interest declared.	None declared. No conflict of interested declared.
Follow-up period	At two weeks, one month, three months and six months of PVT treatment. No follow up after six months of treatment.	All patients were followed for at least three months after initiation of anticoagulation. Mean duration of follow-up was 41.6 months. Mean duration of follow-up varied across groups, with the longest duration in the warfarin group (55.8 months) and the shortest in the DOAC group (28.1 months)	Every seven days with questionnaires focused on symptoms of bleeding Abdominal ultrasonography performed every two weeks during treatment until recanalisation and then every two months for one year to detect any recurrence of thrombi.	Patients were followed up at three months and six months. No follow up after six months.
Outcome	Treatment with edoxaban resulted in significant reduction in PVT size. 1.42cm^3 at two weeks and 0.42cm^3 at six months (P=0.016). Treatment with warfarin resulted in increased PVT volume from 1.73cm^3 at two weeks to 2.85cm^3 at 6 months. INR control was achieved in only 57% of patients (P=0.005). Results are clearly defined and are attributed for initial number of patients enrolled.	Treatment with DOACs was associated with the highest complete radiograph resolution rates: Dabigatran – 75%; n=6 Apixaban – 65%; n=13 Rivaroxaban – 65%;n=42 Enoxaparin was associated with a CRR rate similar to that of the DOACs (57%; n=40). Warfarin was associated with worse outcomes in this regard (CRR rate, 31%; n=33). INR control was achieved in only 62% patients.	Treatment with rivaroxaban showed rapid resolution and complete recanalisation of acute PVT within 2.6 +/– 2.0–3.8 months in 34 patients (85%). Six patients showed delay and partial resolution (of >50% of lumen). None experienced recurrence of PVT. Treatment with warfarin showed complete recanalisation in 18 patients (45%). Recurrence occurred in 22% of patients (n=4) who previously showed complete recanalisation.	Treatment with DOACs after three months showed complete or partial recanalisation of PVT in 12.8% patients (n=5). Treatment with DOACs after six months showed complete or partial recanalisation of PVT in 28.2% (n=11). All patients enrolled into study accounted for and death/side effects/reason for termination in study is described. One patient in DOAC group decided to exit study after developing 13 days of melena while taking rivaroxaban.
Adverse effects	Clinically significant gastrointestinal bleeding in 15% in edoxaban group (n=3) vs 7% of warfarin group (n=2). Paper does not divulge what is considered significant and the outcomes of these patients.	Individual bleeding events per anticoagulant are not reported. However, paper reports when grouped in aggregate, DOACs were associated with a lower risk for major bleeding relative to warfarin. Twelve patients (3.6%) died during follow-up and mortality did not significantly differ across groups. Three of these deaths were related to PVT. These deaths were in patients that received enoxaparin, warfarin or no-anticoagulant. Individual cause of death in DOAC arms are not described.	No major bleeding in rivaroxaban arm. In control arm 9 patients (41%) developed moderate ascites, 17 patients (43%) experienced severe upper GI bleeding. Death occurred in 8 patients (36.4%) after 2.3 +/– 0.8 months attributed to uncontrolled upper GI bleeding. Criteria for major adverse effects is clearly defined in paper.	Dabigatran: Haematuria (n=1) – Resolved after reducing dose to 150mg daily. Rivaroxaban: Haemoptysis (n=1) – Resolved after dose reduced to 10mg daily Melena (n=1)

PVT: portal vein thrombosis; DOACs: direct oral anticoagulants; HCV: hepatitis C virus; INR: international normalized ratio; CT: computed tomography; S/C: subcutaneous