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Original Article

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Complications in hepatic vein catheterisation and transjugular liver biopsy

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ABSTRACT

INTRODUCTION. Portal pressure predicts the occurrence of decompensations in cirrhosis. Portal pressure is primarily measured via hepatic vein catheterisation (HVC), to which a transjugular liver biopsy (TJLB) may be added. Indications for HVC are mainly therapy control and prognosis. TJLB is performed when a percutaneous liver biopsy is contraindicated or for other diagnostic reasons. Both procedures have reported low complication rates. The aim of this study was to identify indications and 30-day postprocedural complications.

METHODS. Based on procedure codes, a list was generated in the report database comprising procedures from 1 January 2018 to 31 January 2022. Procedures were identified in electronic charts (Cosmic Arkiv). A total of 209 patients undergoing 277 procedures were included. Information regarding indications, complications, age, sex, diagnosis, comorbidity and blood tests was also analysed.

RESULTS. The more frequently reported indications for HVC were control of betablockers and diagnosis. Indications for TJLB were diagnostic and research purposes. Complications after HVC included pain and transient supraventricular arrhythmias. Four major complications after TJLB were found, which led to admission due to various causes of bleeding.

CONCLUSION. HVC and TJLB are safe procedures. The complication rate for HVC and TJLB was 3.3% and 6.8%, respectively. Complications were minor; only four major complications after TJLB were found - none of which were mortal.

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Liver cirrhosis is the end stage of chronic liver diseases. Advanced disease is characterised by decompensations. Decompensations and prognosis may be predicted by portal pressure as portal hypertension (PHT) may lead to ascites, variceal haemorrhage and hepatic encephalopathy (HE), among others [1-3]. This causes further complications or death [1, 3-5]. PHT may be divided into pre-, intra- or post-hepatic hypertension. Cirrhosis due to parenchymal liver diseases results in intrahepatic PHT [1, 2]. PHT may be estimated using different techniques, including hepatic vein catheterisation (HVC), platelet count, transient elastography and portal vein catheterisation [2, 3, 5, 6]. The most used estimate is measurement of the hepatic venous pressure gradient (HVPG), which is obtained via HVC [2]. HVC can be done by using any of the following three access veins; the jugular, femoral or brachial vein [2, 5, 6].

HVPG is the difference between the free and the wedged hepatic venous pressure [2, 5]. Clinically significant PHT is defined as HVPG > 10 mmHg, which is associated with complications [1-3].

Indications for HVC are diagnosis of PHT, prognosis, risk stratification, response to antiviral/betablockade treatment and assessment of operability in patients with hepatocellular carcinoma (HCC) [1, 2, 5]. HVC is safe and complications are rare [2]. Complications include damage to the access vein; leakage, haematoma, arteriovenous fistula or Horner syndrome [2, 6]. Transient supraventricular arrhythmias and vagal reactions are seen in some patients [2, 5, 6]. Ultrasound (US) guidance improves the precision of venous puncture and reduces the risk of procedural complications [2, 6].

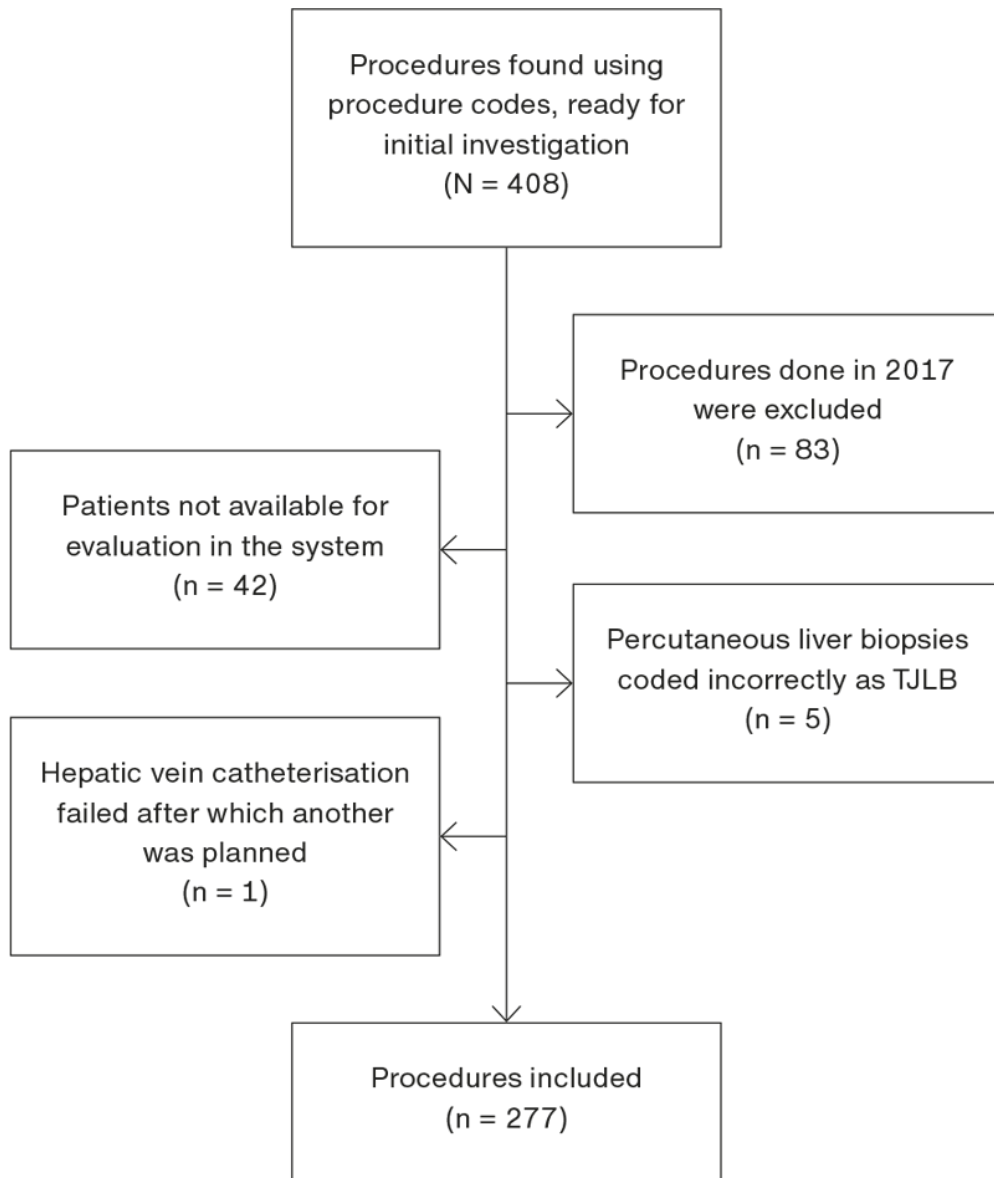
If needed, a transjugular liver biopsy (TJLB) may be added to an HVC when adopting a transjugular approach [2, 5, 6]. TJLB is preferred in patients with ascites, severe coagulopathy or obesity in whom a percutaneous liver biopsy (PLB) may be contraindicated. TJLB is also added to HVC if a patient is under diagnostic investigation for PHT [7, 8]. PLB is the standard way of obtaining a liver biopsy. The major complication rate is reported to be up to 8% after PLB, where pain is reported to arise in up to 50% [9]. The complications listed are pain, bleeding, organ puncture, fistulas and non-target biopsy. Excessive bleeding or bile peritonitis after PLB may lead to mortality [9]. US guidance reduces complications [9]. TJLB is reported with a lower complication rate (up to 7.1%) of which major complications account for 0.59% and minor complications for 6.5% [7, 8]. The complications listed are abdominal pain, haematoma (cervical, intrahepatic), fistulas, bleeding, puncture of surrounding vessels/organs, accidental puncture of the jugular artery, pneumothorax, supraventricular/ventricular arrhythmia and non-target biopsy [7, 8]. The transjugular approach reduces the bleeding risk as it does not puncture the liver capsule. However, liver capsule puncture is seen after TJLB [7, 8].

The aim of this study was to describe indications in the current cohort for HVC and TJLB over a five-year period. Besides, we determined postprocedural complications within 30 days of HVC with or without TJLB among adults with suspected or known liver disease. We hypothesised that no crucial complications were associated with the procedures.

METHODS

This was a quality assurance study. We included patients who underwent HVC with or without TJLB at the Department of Gastroenterology and Hepatology, Odense University Hospital, Denmark, from 1 January 2018 to 31 January 2022. Inclusion procedures are shown in **Figure 1**. A total of 209 patients undergoing 277 procedures were analysed; 57 patients underwent multiple procedure; 47 patients underwent two, nine underwent three and one underwent four procedures. Patients with cirrhosis were divided into Child-Pugh (CP) groups based on albumin, bilirubin, international normalised ratio (INR), ascites, and hepatic encephalopathy (HE).

FIGURE 1 Flow chart depicting the procedures included in this study.



TJLB = transjugular liver biopsy.

Data collection

Data were collected in the report database based on the procedure codes “BMBZ50C” for HVC and “KJJA26” for TJLB. Permission to assess the patients’ data was given by the Director.

Data were found based on the patients’ social security number. Information was obtained from the electronic chart “Cosmic Arkiv on procedures, indications, complications, age, sex, diagnosis, comorbidity and CP groups. Patients were registered with a diagnosis and comorbidity at every procedure. Therefore, more diagnoses than

patients were found. An online biochemistry service “BCC-web” was used for blood tests. Blood tests dated within three months from baseline were used. Data on comorbidity were found based on patient records and use of medication. Some patients did not have blood tests within the time criteria, and CP scores noted in the journal were therefore used instead.

In patients with several medical records, information about ascites, HE and comorbidity was searched for.

Objectives

The primary objectives were indications for and complications after HVC and TJLB. The indications for HVC were divided into five groups: research, diagnosis, non-selective beta-blocker (NSBB) response, transjugular intrahepatic portosystemic shunt (TIPS) and other. The indications for TJLB were divided into diagnosis or research purposes.

HVC complications were divided into four groups: none, pain, jugular haematoma and other. TJLB complications were divided into six groups: none, pain, bleeding, admission, pain and admission, and bleeding and admission.

Patients were divided into groups based on their diagnosis: alcoholic cirrhosis, other cirrhosis and no cirrhosis. Patients with suspected cirrhosis were diagnosed by biopsy or based on clinical presentation. Comorbidity was divided into four groups: diabetes mellitus, heart disease, lung disease and other. Other comorbidities were mostly treatment with anticoagulants without an indication, hypertension, hypothyroidism and patients with HCC.

Statistical analysis

Data are presented as descriptive statistics. The numbers presented are in relation to number of procedures. Age is reported in relation to number of patients. Categorical data are presented as percentages of observations. Numerical data are presented as medians with interquartile range or means with standard deviations depending on whether the data are normally distributed or not.

Ethics

Data were found based on procedure codes. Therefore, patients were not required to sign a declaration of consent. Data were handled anonymously.

Trial registration: not relevant.

RESULTS

Baseline data are shown in **Table 1**. A total of 209 patients undergoing 277 procedures were included; 274 procedures were done using the jugular vein, and three were done using the femoral vein. The median age was 61 years, 65% were men.

TABLE 1 Baseline characteristics for patients undergoing hepatic vein catheterisation with or without transjugular liver biopsy.

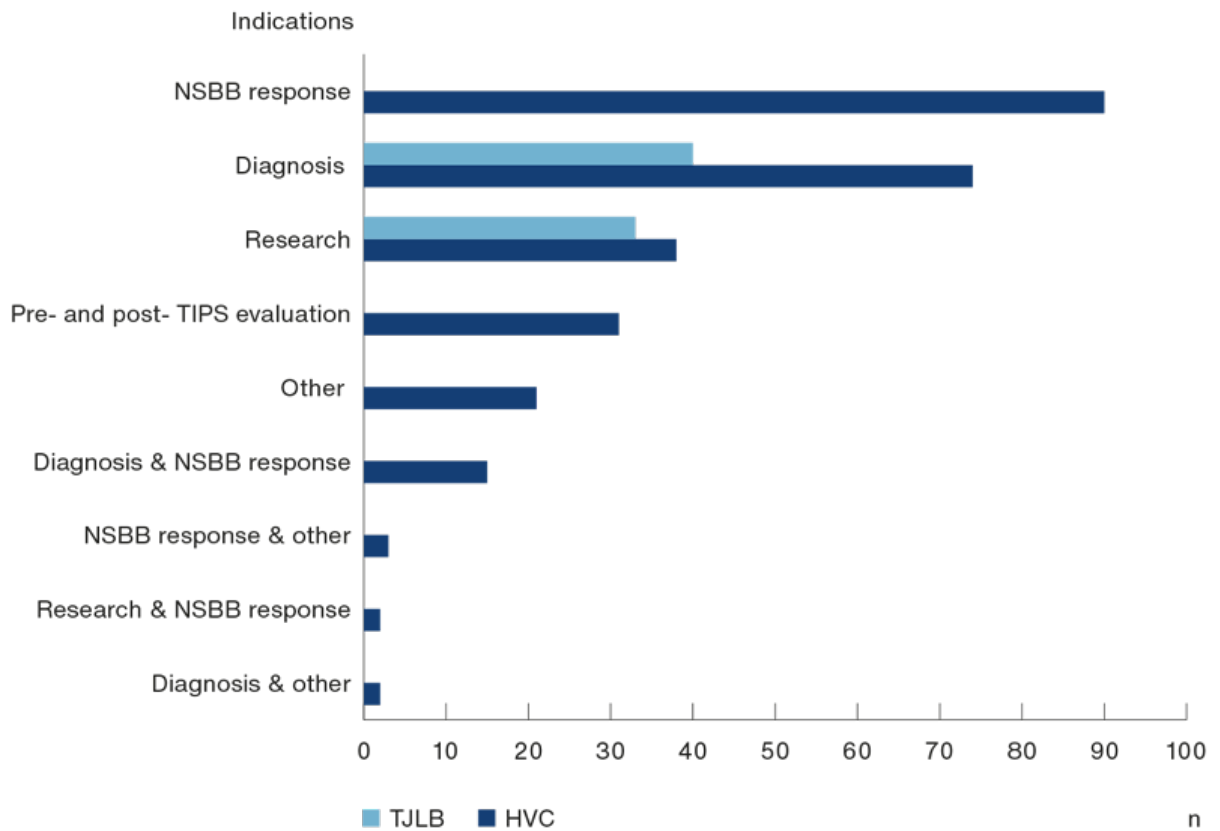
Age, median (IQR), yrs	61 (51-66)
<i>Procedures, n (%)</i>	
Transjugular access	274 (99)
Femoral access	3 (1)
Subtotal	277
Hepatic vein catheterisation, n (%)	188 (68)
Hepatic vein catheterisation with transjugular liver biopsy, n (%)	88 (32)
Only transjugular liver biopsy, n (%)	1 (0.4)
<i>Patients, n (%)</i>	
Male	135 (65)
Female	74 (35)
Subtotal	209
<i>Diagnosis, n (%)</i>	
Alcoholic cirrhosis	103 (37)
Other cause of cirrhosis	75 (27)
Alcoholic cirrhosis and other cirrhosis	17 (6)
Alcoholic cirrhosis and other diagnosis	2 (0.7)
No cirrhosis	79 (29)
No information	1 (0.4)
<i>Comorbidities, n (%)</i>	
Diabetes, type 1 and type 2	27 (10)
Heart disease	9 (3)
Lung disease	8 (3)
Other	78 (28)
0 comorbidities	64 (23)
2 comorbidities	74 (27)
3 comorbidities	14 (5)
4 comorbidities	2 (0.7)
No information	1 (0.4)
Hepatic venous pressure gradient, median (IQR), mmHg	13 (7-18)
<i>Child Pugh Score, n (%) (N = 197)</i>	
A	103 (52)
B	61 (32)
C	16 (8)
No information	17 (9)
Haemoglobin, mean (± SD), mmol/l	7.9 (± 1.5)
Thrombocytes, mean (± SD), × 10 ⁹ /l	146 (± 79)
Alanine transaminase, mean (± SD), U/l	51 (± 126)
Bilirubin, mean (± SD), µmol/l	26 (± 46)
Albumin, mean (± SD), g/l	39 (± 6)
INR, mean (± SD)	1.29 (± 0.31)

INR = international normalized ratio; IQR = interquartile range; SD = standard deviation.

Primary results

HVC and TJLB indications are shown in **Figure 2**. A total of 22 procedures had more than one indication. Indications for HVC reported with “other” accounted for preoperative evaluation and monitoring. Four HVCs failed due to procedural errors. There were only two indications for TJLB: diagnosis and research purposes; 16 biopsies were planned but failed. Frequent causes of failure included that the operator refrained from biopsy due to various reasons, e.g., inability to cooperate (non-sedated patients), technical problems and normal HVPG measurement. For one patient, it was not possible to find data on diagnosis and comorbidity.

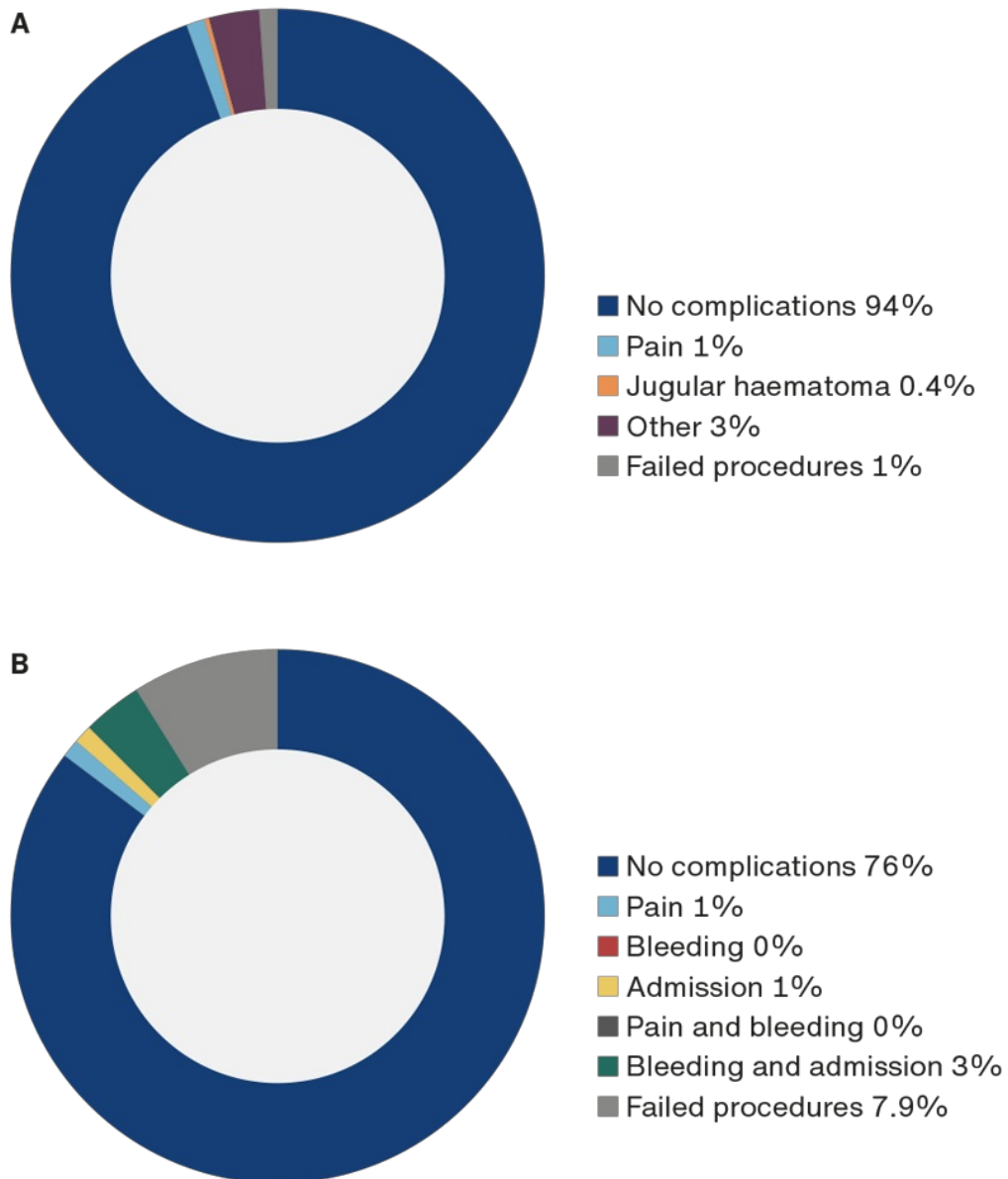
FIGURE 2 Indications for hepatic vein catheterisation (n = 276) and transjugular liver biopsy (n = 89).



HVC = hepatic vein catheterisation; NSBB = non-selective beta-blockers; TIPS = transjugular intrahepatic portosystemic shunt; TJLB = transjugular liver biopsy.

Complications after HVC are shown in **Figure 3**. The complication rate was 4%. Two patients were admitted due to femoral access. When adjusting for these two and the failed procedures, the complication rate was 3.3%. Four patients experienced transient supraventricular arrhythmias. One had a suspected pseudoaneurysm, which was later disproved.

FIGURE 3 30-day post procedure complications and failure rates for hepatic vein catheterisation (n = 276) (A) and transjugular liver biopsy (n = 89) (B).



Complications after TJLB are shown in Figure 3. Some patients were admitted after biopsy for research purposes or following protocol. Since no complications were found, these cases were not reported as admissions. Four major complications were found. Three patients were admitted due to bleeding (two with haemobilia, one with minor capsule perforation) and one was admitted due to a gallbladder perforation. The complication rate was 5.6%. After adjusting for failed procedures, the complication rate was 6.8%.

The risk of complications was not related to CP scores or biochemical findings.

Secondary results

The median HVPG measurement was 13 mmHg. In 103 procedures, the patients had alcoholic liver cirrhosis, 75 had non-alcoholic cirrhosis and 79 had no cirrhosis. A total of 22 had more than one diagnosis: 17 with combined cirrhosis and two with alcoholic cirrhosis and another diagnosis. A total of 197 had a cirrhosis diagnosis, but only 180 could be divided into CP groups as information was not found in relation to the remaining procedures.

DISCUSSION

In this study, 277 procedures were included of which 188 were HVCs, 88 were both HVC and TJLB and one was a TJLB. The main indications for HVC in this study were NSBB response, diagnosis and research purposes. Indications for TJLB were diagnosis and research purposes. We found that cirrhosis was the main diagnosis. Among these cases, 53% were due to excessive alcohol consumption. Only four major complications after TJLB were found in this study.

Hepatic vein catheterisation

Many studies agreed that HVC is used for diagnosis and classification of PHT, treatment response and prognosis [1-3, 5, 6]. Other studies have listed other indications such as assessment of a new therapy and preoperative evaluation [2, 6]. All indications mentioned were found in this study besides response to antiviral treatment and assessment of a new therapy. The primary indications found in this study were NSBB response, diagnosis and research purposes. Another indication was evaluation following TIPS. Combined indications were also found.

HVC is an invasive procedure but is considered safe and associated with a low complication rate. Complications are minor and primarily related to the access vein [2, 5, 6]. One jugular haematoma was found without any further complications. Another minor complication is pain, which was experienced by three patients in this study. Transient supraventricular arrhythmias are listed as a complication during the procedure [2, 6]. This was experienced by four patients in this study. Two patients required monitoring at the cardiology ward.

Minor complications, such as pain and supraventricular arrhythmias, were probably underreported in this study because the complications were analysed retrospectively. Regarding major complications, underreporting is not suspected because major complications require admission and will therefore be reported in the charts.

Transjugular liver biopsy

As mentioned in other studies, a proportion of the biopsies were done for diagnostic reasons [8, 10]. In this study, we did not specify the diagnostic indications. Other studies primarily listed indications for TJLB as conditions that contraindicate a PLB [7, 8]. Indications from two other studies [10, 11] also included other indications such as pre- and post-transplant evaluation, and conditions with a high bleeding risk. A study by Dohan et al. [10] listed acute alcoholic hepatitis as the main indication for TJLB. All the listed indications were also found in our study.

Major complications after TJLB were reported in 0.56-3% [7, 8, 10, 11] of cases. In this study, we found a major complication rate of 5.5% as admissions were counted as a major complication. One reason for the discrepancy may be that the procedure was newly introduced at the hospital and therefore the operators lacked experience.

Besides, the number of TJLBs was small in this study with 89 TJLBs and four major complications. The complication rate will be relatively higher than in other studies, e.g. the study by Dohan et al. [7] which found two major complications in 341 patients and a 0.59% complication rate. TJLB is reported with a lower complication rate than PLB. In the article by Knawy & Shiffman [9], the authors compared complications between blind PLB and US-guided PLB. Major complications reported after blind PLB were up to 6.5% but

reduced to 2.6% when using US. The corresponding figure is 0.56-3% after TJLB [7, 8, 10, 11]. Biopsy pain after blind PLB was reported up to 50% but decreased to 37.5% when using US [9]. In the study by Dohan et al. [7], pain after TJLB was found in 10.26%.

TJLB is performed in patients with more advanced disease compared to PLB. Therefore, TJLB may be considered an even safer procedure than visualised by the listed complication rates.

The failure rate for TJLB was reported to fall in the 3.2-8% range in other studies [7, 8, 10, 11]. We have similar findings with a procedural failure rate of 7.9%. However, a total of 18% planned TJLBs failed. In the remaining 10.1% of cases, the biopsy was cancelled for clinical reasons.

Limitations

This study has several limitations. The study was retrospectively evaluated. Consequently, some data on complications may not have been registered in the journals.

Besides, the procedures examined were performed only at Odense University Hospital. Completion of the procedures and the failure rates rely on the operator. Therefore, complication and failure rates could be different from those of other operators. However, indications should be similar. To evaluate if it is possible to lower the complication rate, further research based on procedures from all operating centres in Denmark is warranted.

A total of 42 patients were excluded due to missing information. Missed procedures may potentially cause an under- or overestimation of the complication rate. Besides, the small study population may lead to underestimation of complication rates. Another limitation is that only one researcher evaluated the patients' data.

CONCLUSION

The most frequent indications for HVC found in this study were assessment of NSBB response, diagnosis and research purposes. For TJLB, the indications were diagnosis and research purposes. Complications after HVC were minor. Pain and transient supraventricular arrhythmias were the most frequently found complications. TJLB may be associated with major complications. However, this is rare and only 4.5% of cases in our study experienced a major complication. No complications were associated with mortality. Findings from this study may be used for patient information before the procedure. Due to the small study population, our results may be biased.

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