Original Article

Retrospective analysis of post-operative coagulopathy after major hepatic resection at a tertiary care centre in Northern India

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ABSTRACT

Background and Aims: Hepatic resection is a major surgery associated with intraoperative massive fluid shifts, blood loss, haemodynamic instability and risk of development of post-hepatectomy liver failure. Hepatic resection predisposes the patient to coagulopathy as well as venous thrombosis. However, due to the development of deranged coagulation profile post-operatively, there is a dilemma in starting thromboprophylaxis. Our aim in this study was to determine the incidence of coagulopathy in patients undergoing major hepatectomy. **Methods:** In this retrospective study, we included 86 patients who had undergone major hepatectomy between January 2010 and December 2015 at our centre. Intraoperatively, we noted the number of liver segments resected, details of epidural catheter insertion, estimated blood loss, transfusion requirement and need for mechanical ventilation post-operatively. Trends of international normalised ratio (INR) and platelet values were recorded until post-operative day 5. **Results:** Of the 86 patients, 6 (7%) had an abnormal coagulation profile pre-operatively and 39 (45.34%) patients developed a derangement in their coagulation profile on 1st post-operative day (POD). Platelet count was significantly lower and INR values were significantly higher than the pre-operative values on all 5 PODs. Sixty-seven (78%) patients had pre-operative epidural catheter insertion for post-operative pain management. Mechanical thrombophylaxis was used routinely. **Conclusions:** The incidence of post-operative coagulopathy in our patients who underwent major liver resection was 45.34%. Epidural catheters could be removed safely without transfusion between POD 5 and 7. There was no incidence of venous thrombosis or thromboembolism.

Key words: Coagulopathy, hepatectomy, thromboprophylaxis, venous thrombosis

INTRODUCTION

Surgery on the liver is a complex operative intervention associated with high morbidity and mortality. It is a challenge because of its unique anatomic architecture and the wide range of vital functions it performs. Liver resection is associated with intraoperative massive fluid shifts, blood loss, haemodynamic instability and development of coagulopathy. A number of factors contribute to the altered coagulation status after major liver resection. These include preexisting liver dysfunction, extent of intra-operative blood loss, remnant liver volume and ischaemia-reperfusion injury.[1]

Patients with preexisting liver disease who require surgery are at greater risk for surgical and anaesthesia-related complications than those with a healthy liver. Most studies in literature comment on incidence of coagulopathy post-liver resection in

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healthy donors. Literature describing the effect of liver resection in diseased liver is limited.[2]

Major liver resection involves resection of three or more segments of the liver and minor liver resection is defined as a resection of two or fewer hepatic segments.[3] The liver mass remaining post-resection is important as majority of the coagulation factors are synthesised in the liver. Epidural analgesia following major abdominal surgeries helps attenuate stress response, prevents post-operative pulmonary atelectasis and attenuates the hyper-coagulable response to surgery. By decreasing post-operative opioids requirement, it also reduces the incidence of post-operative ileus and helps reduce hospital stay. It preserves post-operative immune function by attenuating the surgical stress response and thus maintains a competent immune system.[4] However, the risk of development of coagulation abnormalities following liver resection limits its practical usage.

Patients who undergo liver resection are also at risk of development of venous thrombosis. In one study, the incidence of venous thromboembolism (VTE) was 14.3% in patients with a peak post-operative international normalised ratio (INR) ≥1.5, compared to 3.6% in patients with a peak INR ≤1.5.[5]

However, due to the development of deranged coagulation profile post-operatively, there is a dilemma in starting thromboprophylaxis.[6] The primary objective of this study was to assess the incidence of coagulopathy in patients undergoing major hepatectomy at our tertiary care centre. The secondary objective of this study was to assess the safety of inserting epidural catheter after liver resection.

METHODS

Following Ethical Committee approval from the Institutional Review Board, we performed a retrospective review of all patients who had undergone open major hepatic resection at our hospital between January 2010 and December 2015. Computerised surgical lists were used to compile the list of subjects who underwent open major hepatectomy. Data were collected from patient's clinical charts, operation records and also by computerised hospital information system. Patients with missing data were excluded from the study. Other exclusion criteria were surgeries in which the decision was made intraoperatively to abandon hepatic resection and donor hepatectomies for live donor liver transplant.

Pre-operative data included patient characteristics, underlying surgical pathology and coagulation profile (INR and platelet counts).

Intraoperative data included number of segments resected, details of epidural catheter insertion, estimated total blood loss and transfusion of blood products and whether the patient was extubated on table or the patient was shifted to intensive care for further mechanical ventilation.

Post-operative data collected included INR and platelet values until post-operative day 5. The patient was considered to have abnormal coagulation profile if INR >1.5 or/and platelet count <100,000/cu mm.[7,8]

We tried to ascertain existence of any association between pre-operative coagulation profile, number of segments resected, intra-operative blood loss and its effect on post-operative coagulopathy. The day of removal of epidural catheter post-operatively was noted along with documentation of bleeding or discharge from insertion site.

Data analysis was performed using SPSS for Windows 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to derive means and percentages. The risk factors defined *a priori* were evaluated for an association with an abnormal post-operative coagulation profile. The comparison between patients with coagulopathy and without coagulopathy was done using Student's *t*-test or Mann–Whitney test in case of continuous data. The categorical data were analysed using Chi-square or Fisher's exact test. To see the change over a period in coagulation parameters, repeated-measures analysis was carried out followed by post-operative comparison by least significant difference method. A $P < 0.05$ was considered statistically significant.

RESULTS

Eighty-six patients met the inclusion criteria during the period of review [Figure 1]. Of these, 53 were male and 33 were female. The most common pathology was hepatocellular carcinoma ($n = 40$ followed by hilar cholangiocarcinoma ($n = 17$) [Table 1].

Of the 86 patients, 6 (7%) had an abnormal coagulation profile pre-operatively and 39 (45.34%) patients developed a derangement in their coagulation profile on 1st post-operative day (POD) which was

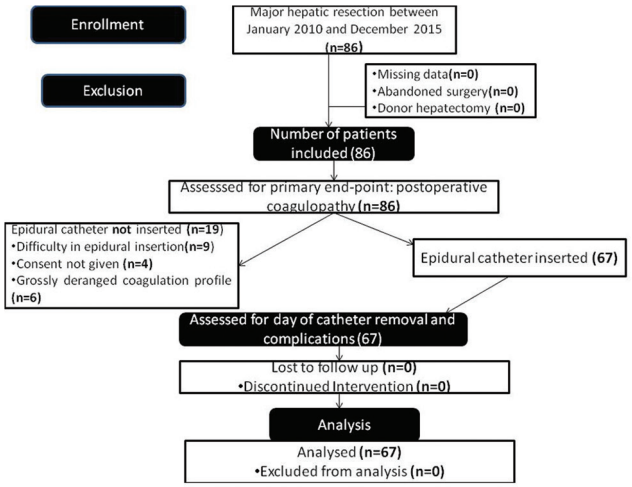

Figure 1: Consort diagram

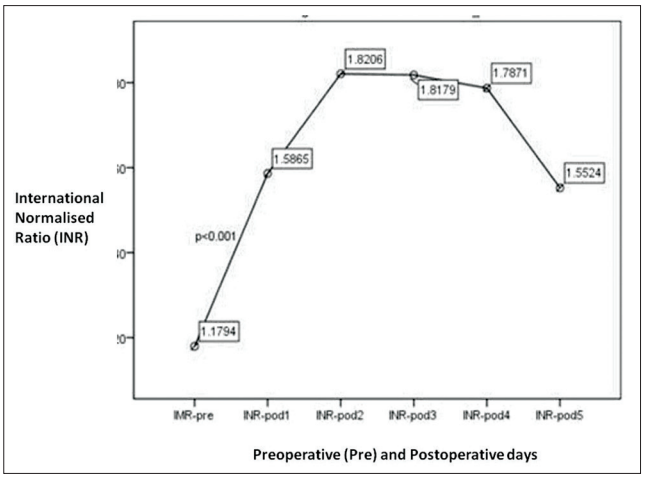

Figure 2: Trends of international normalised ratio (INR) against preoperative (pre) and post-operative (pod) days

statistically significant [Figures 2 and 3]. INR values were significantly higher on POD 1 when compared to pre-operative values. INR values reached a peak on POD 3 and POD 4 and decreased from POD 4 onward. INR values were significantly higher than the pre-operative values on all five PODs ($P < 0.001$) [Figure 2].

Similarly, platelet counts were decreased significantly on POD 1 when compared to pre-operative values. Platelet count was significantly lower than the pre-operative values on all 5 PODs ($P < 0.001$) [Figure 3].

Of the 86 patients, forty-five were extubated on table at the end of surgery. The rest were electively ventilated due to prolonged duration of surgery (>8 h) and for haemodynamic stabilisation.

Fifty-seven percent of the patients ($n = 49$) underwent resection of four segments and fifty-eight percent of patients ($n = 50$) had a blood loss of more than 1000 ml [Table 2]. The average blood loss during the surgery was 1157.6 ml.

Sixty-seven patients had pre-operative epidural catheter insertion for post-operative pain management. Epidural catheter insertion was deferred for various reasons such as difficulty in insertion ($n = 9$), consent was not given by patients for epidural placement ($n = 4$) and grossly deranged coagulation profile ($n = 6$) in the rest [Figure 1].

Epidural catheter was removed on POD 5 but was delayed in 5 patients up to POD 7 because of deranged coagulation profile. Epidural catheter was not removed under fresh frozen plasma cover

Table 1: Demographics and diagnosis of patients undergone major hepatectomy

Parameter	Values
Age (mean±SD)	51±16
Gender (No. of male:female)	53:33
Diagnosis	***N* (%)**
Hepatocellular carcinoma	40 (46)
Cholangiocarcinoma	17 (19.8)
Carcinoma gallbladder	8 (9.3)
Haemangioma	6 (7.0)
Metastasis	5 (5.8)
Hydatid cyst	4 (4.7)
Benign biliary stricture	2 (2.3)
Others	4 (4.7)
Total	86 (100)

Table 2: Number of segments resected and blood loss

Parameters	Values
Number of segments	***N* (%)**
3	4 (4.7)
4	49 (57.0)
5	25 (29.1)
6	8 (9.3)
Blood loss (mL)	***N* (%)**
<500	13 (15)
500-1000	23 (27)
>1000	50 (58)

in any of the patients. None of the patients had any bleeding, oozing, catheter site infection or mention any paraesthesia or neurological deficit and accidental removal of epidural catheter in the records scrutinised. There was no significant association found between the amount of blood loss (patients with coagulopathy [1223.44 ± 901.49 ml] and without coagulopathy [965.91 ± 562.39 ml; $P = 0.21$]), number of segments resected (patients with

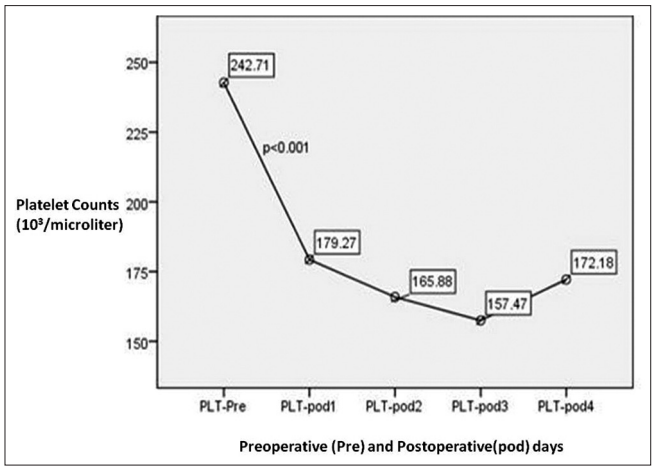

Figure 3: Trends of abnormal platelet counts against preoperative (pre) and post-operative (pod) days

coagulopathy [4.47 ± 0.75] and without coagulopathy [4.32 ± 0.64; $P = 0.37$]) and age of the patient (patients with coagulopathy [51.84 ± 15.95] and without coagulopathy [47.15 ± 17.49; $P = 0.25$]) with respect to the post-operative coagulation profile.

DISCUSSION

In the present study, incidence of post-operative coagulopathy was 45.34% in patients who underwent major liver resection.

In another retrospective study,[3] an abnormal coagulation profile was present in 58.2% of the patients underwent open hepatectomy during post-operative period. Twenty-three percent of their study population had preexisting cirrhosis; however, only 35% of the study population underwent major hepatic resection. All patients included in our study underwent major liver resection. However, since only 6% of the study population was cirrhotic, incidence of post-operative coagulopathy was lower in our study although pre-operative coagulopathy was present in all with underlying cirrhosis. The criteria used to define abnormal coagulation profile were also different in their study. A prothrombin time >11.2 s or partial thromboplastin time >36.1 s or platelet count <100,000/mm^3 was considered as an abnormal coagulation profile. An independent association was found between pre-operative liver cirrhosis and post-operative coagulopathy. In our study, only 6% of the study population was cirrhotic which may be responsible for the lack of association between pre-operative cirrhosis and post-operative coagulopathy. Similar to their study, we too found an increase in coagulopathy on the first 3 PODs, which gradually returned to normal. In our study, we included only major liver resections.

The duration of vascular occlusion used to limit blood loss during parenchymal dissection also has been suggested as a contributing factor to post-operative coagulopathy.[9] In the present study, vascular occlusion techniques were not used. In our centre, cavitron ultrasonic surgical aspirator is used for parenchymal resection as it is associated with low blood loss, a better safety record, with low risk of bile leak. It is particularly useful in major hepatic resections when dissection of the major branches of the hepatic veins is required as it allows clear dissection of the hepatic vein from the tumour.[10]

It has been described that liver cirrhosis increases the risk of an abnormal post-operative coagulation profile.[3] This worsens in the late post-operative period (POD 5 onward) and becoming nearly double that of the early post-operative period (POD 1to 5) (odds ratio 6.84 vs. 3.73), when the epidural catheter is usually planned for removal.[3] In the present study, five patients had cirrhosis along with hepatocellular carcinoma and all of them had deranged pre-operative coagulation profiles. At our centre as a protocol, epidural catheterisation is not attempted in patients with INR >1.5 and/or platelet count of <100,000/cu mm. Hence, in six patients, epidural catheterisation was not considered.Consent for epidural placement was not given by four patients, and in nine other patients, it was attempted but abandoned due to difficulty in placement.

In a similar study on 136 patients who had undergone major and minor hepatic resection, significant changes in disturbances of coagulation profile were observed.[11] In patients who underwent minor liver resection, coagulation profile returned to control value within 1 day. However, in patients who underwent major liver resection, the disturbances in coagulation profile were profound and prolonged and a return to the pre-operative value was achieved by day 5.[11] The median duration of epidural analgesia in their study was 3 days. However, epidural catheters were not removed for 7 days in six patients (9%), who underwent major resection due to disturbed coagulation profile. No patient developed signs or symptoms of spinal haematoma.[11] In our study, where only major liver resection was done, epidural catheter was removed on POD 5 in all patients except five patients, in whom it was removed on POD 7, after normalisation of INR.

No catheter site haematoma, bleeding, collection or oozing was observed in any patient. There was no neurological complication due to epidural placement. Since the reported incidence of epidural haematoma in itself very low (1 in 168,000),[12] the small number of cases included in our study is not enough to evaluate safety with respect to epidural haematoma post-hepatectomy, and the decision to insert and remove epidural catheters needs to be individualised.

In the present study, all patients received mechanical thromboprophylaxis in the form of intermittent pneumatic compression devices throughout the duration of the surgery and also during post-operative stay until they were mobile. No pharmacological thromboprophylaxis was given because of the fear of bleeding. There are various studies supporting as also against thromboprophylaxis after hepatic resection. The prevalence of post-operative VTE in general surgery patients is 15%–40% and is associated with significant morbidity, mortality and increased length of hospital stay.[13]

Early mobilisation, intermittent pneumatic compression devices and pharmacologic agents are used to prevent VTE. Pharmacologic thromboprophylaxis is recommended for most general surgery procedures, but the fear of bleeding after major hepatectomy has limited its use.[14] However, recent evidences show that hepatectomy patients are in fact hyper-coagulable. Many factors including tissue damage, reduced synthesis of clotting factors by the remnant liver and blood loss are considered the reason for the hyper-coagulability.[13,14] In our cohort of patients, there was no report of thromboembolism.

Limitations of this study were its restrospective nature with small number of cases and use of conventional coagulation parameters alone for assessing status of coagulopathy. Viscoelastic methods of analysing the coagulation status and guiding transfusion practices such as thromboelastogram and rotational thromboelastometry were not used to define abnormal coagulation profile in this study.[15] However, these tests are often not available and conventional coagulation parameters continue to be used.

CONCLUSIONS

Post-operative coagulopathy occurred in 45.34% of our patients who underwent major liver resection irrespective of pre-operative coagulation status, number of segments resected and the underlying aetiology. Epidural catheter insertion and removal appears to be safe, and conventional coagulation studies can be used to guide the removal. However, the number of patients with underlying cirrhosis was too small to establish the safety of the procedure in patients with cirrhosis.

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Conflicts of interest

There are no conflicts of interest.

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