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Outcomes of Portal Vein Tumour Thrombosis [PVTT] with Or Without Anticoagulation In 13 Patients Following in Vascular Department, Ttsh, Singapore

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1. Abstract

1.1. Aim: To look at the clinical outcomes in portal vein tumour thrombosis [PVTT] with or without anticoagulation.

1.2. Method: This study was approved by ethics committee. Patients following up in Vascular department were recruited with retrospective analysis from 2011 to 2016. Patients were classified into 3 groups: Portal vein thrombosis [PVT] with cirrhosis, malignancy, and infections. The biggest group was PVT with malignancy also known as portal vein tumour thrombosis [PVTT]. This group was analysed in this study. Statistical analysis was done with frequency, means, and percentages were calculated. Outcome measures were defined as clot resolution with or without anticoagulation, bleeding, recurrence, death.

1.3. Results: Out of 30 patients of PVT, 13 patients of PVTT were analysed in this study. They were primary hepatocellular carcinoma [HCC] in 4 and secondary HCC in 9 patients.

Mean age was 66.8 years [range of 47-91 years]. There were 6 [46.2%] males and 7 [53.8%] females with ethnicity Chinese in 11 [84.6%], 2 [6.7%] Malay, other races 1 [7.7%].

Six patients received anticoagulation and 7 did not receive anticoagulation.

1.Of 6 patients who received anticoagulation, there was complete resolution of thrombus in 1 [16.7%], partial resolution in 0 [0.0%], no resolution in 5 [83.3%]. There was bleeding in 1 [16.7%], there was no recurrence and 4 [66.7%] died during the period of follow-up.

2.Of 7 patients who did not receive anticoagulation, there was complete resolution of thrombus in 0 [0.0%], partial resolution in 0 [0.0%], no resolution in 7 [100%]. There was bleeding in 0 [0.0%], there was recurrence in 0 [0.0%] and 4 [57.1%] died during the period of follow-up

1.4. Conclusion: Anticoagulation is of marginal benefit in terms of mortality in patient with PVTT. The rate of recurrence is similar in patients with or without anticoagulation, however, PVTT patients with anticoagulation is associated with increased risk of bleeding.

2. Background

Portal vein thrombosis [PVT] is a potentially life-threatening aliment stems from multiple factors, both local and systemic prothrombotic risk factors [1]. Patients may present asymptomatically or within life-threatening intestinal infarction. Conditions including cirrhosis, malignancy [portal vein tumour thrombosis, PVTT], and abdominal infections, may precipitate thrombus formation, and lead to complications of intestinal ischaemia, portal cholangiopathy, portal hypertension, and death [2].

Use of anticoagulants in PVT poses a risk to patients with any aliment because of increased risk of gastrointestinal bleeding with portal hypertension [3]. Current guidelines are unclear on the efficacy of anticoagulant therapy in patients with PVT [4,5].

3. Aim

To look at the clinical outcomes in portal vein tumour thrombosis [PVTT] with or without anticoagulation.

4. Method

This study was approved by ethics committee [Domain Specific Review Board, Singapore]. Data was collected from inpatient blue-letter referrals to department of Vascular Medicine, General Medicine, Tan Tock Seng Hospital, for portal vein thrombosis, over 5 years.

Patients were classified into 3 groups:

1.PVT with cirrhosis

2.PVT patients with primary or secondary liver malignancy

3.PVT patients with intra-abdominal infections

Patients excluded were those with missing data for primary outcome measures or those with overlap of PVT for 2 or more conditions. Demographic data along with various comorbidities including diabetes, hypertension, previous thrombotic events, and hypercoagulable states were collected. Data was also collected for extent of PVT occlusion, and additional vein occlusions. Primary outcomes measures collected were clot resolution, bleeding, recurrence, death in all three groups and overall, with or without anticoagulation. Frequency means, and percentages were calculated and the data across each subgroup were compared with the variables of use of anticoagulant therapy compared with those who did not receive.

5. Results

In total 30 patients were analysed in this study. The biggest group was PVT with malignancy also known as portal vein tumour thrombosis [PVTT]. This group was analysed in this study. The total number of patients in this group were 13. They were primary hepatocellular carcinoma [HCC] in 4 and secondary HCC in 9 patients. Mean age was 66.8 years [range of 47-91 years]. There were 6 [46.2%] males and 7 [53.8%] females with ethnicity Chinese in 11 [84.6%], 2 [6.7%] Malay, other races 1 [7.7%]. The demographics comorbidities, investigations, outcomes as shown in (Table 1-4).

Six patients received anticoagulation and 7 did not receive anticoagulation.

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2. Of 7 patients who did not receive anticoagulation, there was complete resolution of thrombus in 0 [0.0%], partial resolution in 0 [0.0%], no resolution in 7 [100%]. There was bleeding in 0 [0.0%], there was recurrence in 0 [0.0%] and 4 [57.1%] died during the period of follow-up

Table 1: Demographics: PVT with Malignancy

	Overall	No Anticoagulation	Anticoagulation
Count	13	7 (53.8%)	6 (46.2%)
Age: Mean (years)	66.8	67.9	65.5
Age: Range (years)	47 - 91	52 - 91	47 - 77
Gender: Male	6 (46.2%)	4 (57.1%)	2 (33.3%)
Gender: Female	7 (53.8%)	3 (42.9%)	4 (66.7%)
Ethnicity: Chinese	11 (84.6%)	6 (85.7%)	5 (83.3%)
Ethnicity: Malay	1 (7.7%)	1 (14.2%)	0 (0.0%)
Ethnicity: Indian	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ethnicity: Others	1 (7.7%)	0 (0.0%)	1 (16.7%)

Table 2: Comorbidities: PVT with Malignancy

	Overall	No Anticoagulation	Anticoagulation
Total	13	7 (53.8%)	6 (46.2%)
Diabetes Mellitus	4 (30.7%)	1 (14.2%)	3 (50.0%)
Hypertension	8 (61.5%)	4 (57.1%)	4 (66.7%)
Previous Thrombotic Events	2 (15.4%)	1 (14.2%)	1 (16.7%)
Hypercoagulable State	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infection	4 (30.7%)	2 (28.6%)	2 (33.3%)
Cirrhosis	2 (15.4%)	0 (0.0%)	2 (33.3%)

Table 3: Investigations: PVT with Malignancy

	Overall	No Anticoagulation	Anticoagulation
Total	13	7 (53.8%)	6 (46.2%)
Occlusion: Complete	9 (69.2%)	4 (57.1%)	5 (83.3%)
Occlusion: Partial	4 (30.8%)	3 (42.9%)	1 (16.7%)
Additional Occlusion: 1 Vein	4 (30.8%)	3 (42.9%)	1 (16.7%)
Additional Occlusion: 2 Veins	1 (7.7%)	0 (0.0%)	1 (16.7%)
Additional Occlusion: 3 Veins	1 (7.7%)	0 (0.0%)	1 (16.7%)
Intestinal Ischaemia	0 (0.0%)	0 (0.0%)	0 (0.0%)
Portal Hypertension	0 (0.0%)	0 (0.0%)	1 (16.7%)
Portal Cholangiopathy	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thrombocytopenia (Plt <100)	7 (53.8%)	3 (42.9%)	4 (66.7%)
1° Hepatocelluar Carcinoma	4 (30.8%)	2 (28.6%)	2 (33.3%)
2° Hepatocellular Carcinoma	9 (69.2%)	5 (71.4%)	4 (66.7%)

Table 4: Outcomes: PVT with Malignancy

	No Anticoagulation	Anticoagulation
Count	7	6
Resolution: Complete	0 (0.0%)	1 (16.7%)
Resolution: Partial	0 (0.0%)	0 (0.0%)
Resolution: None	7 (100%)	5 (83.3%)
Thrombosis: Complete	2 (28.6%)	1 (16.7%)
Thrombosis: Partial	0 (0.0%)	1 (16.7%)
Thrombosis: None	5 (71.4%)	0 (0.0%)
Bleeding	0 (0.0%)	1 (16.7%)
Recurrence	0 (0.0%)	0 (0.0%)
Mortality Rate	4 (57.1%)	4 (66.7%)
Survival Time: Mean (Days)	90	291
Survival Time: Range (Days)	6 - 219	22 - 981

6. Discussion

The efficacy of anticoagulant therapy in the setting of PVT has been well documented in previous studies. Englesbe et al. also discussed the independent predictive value of an increased age on mortality – with a hazard ratio of 1.02 [confidence interval of 95%] [6]. In our study there was not much difference in age in both groups.

A study by Turnes et al. suggests a rate of 87% for five-year survival of patients receiving anticoagulation therapy [7]. From our data, mortality rates didn't show difference in both groups. Mean survival duration was increased from use of anticoagulants in patients with PVT and malignancy. Prognosis of PVT patients may also be a result of the underlying aetiology of PVT. Patients receiving anticoagulation in malignancy experienced the highest mortality rates amongst the three groups. Mean survival duration was also decreased in patients with underlying malignancy. The effects of thrombus extent on outcomes have been previously studied. Condat et al. related the probability of recanalization [P = 0.003] [8]. An expected increase bleeding risk of patients receiving anticoagulation was observed in all groups of patients. A 2001 study by Condat et al, 84 of 136 patients were treated with anticoagulant therapy, a documented incidence rate of gastrointestinal bleeding was recorded as 12.5 per 100 patient years [95% confidence interval, 10-15][3], however, it was noted by Condat that anticoagulant therapy did not increase the risk of the severity of bleeding. The study concluded by stating that the risk of thrombosis is currently as clinically significant as the risk of bleeding – with the benefit-risk ratio favouring the use of anticoagulant therapy. Our data showed that the use of anticoagulants in patients with PVTT didn't decrease the rate of extension of tumour thrombosis. A decrease in recurrence rates with use of anticoagulation have been documented previously in a study by Huard et al [9]. Findings from our study suggest that with or without the use of anticoagulation, recurrence rate was similar. Prognosis of PVT patients may also be a result of the underlying aetiology of PVT. Patients receiving anticoagulation in malignancy experienced the highest mortality

rates amongst the three groups which we studied. Mean survival duration was also decreased in patients with underlying malignancy, 90 days [three times lower compared to cirrhosis patients]. Use of immediate anticoagulation in non-cirrhotic patients with PVT, especially non-cirrotic and acute, anticoagulation therapy is not only to prevent re-thrombosis but also to prevent extension of the thrombus into the portal venous system [10-14]. Extensive mesenteric vein and portal vein thrombosis has been successfully treated by thrombolysis and anticoagulation [11]. All patients with PVT should be investigated for thrombophilic conditions as possible causes. Therapy for hyop- and hyper-coagulable conditions with low weight heparin should be considered in patients with PVT [15]. Anticoagulants are a safe treatment for PVT and partial or complete recanalization is seen in many patients. However, the benefit to patients from anticoagulation is unclear. [16] This is especially in patients with PVTT. In our study, anticoagulation increased the bleeding risk by 16.67% in patients with PVTT. Our understanding of the aetiology, natural history, and treatment options for extrahepatic PVT have improved over the last few years. The recognition that multiple risk factors, including inherited and acquired thrombophilic predispositions, are involved in the majority of cases merits a methodical search for these, as their identification may influence management [17]. Rare case of massive upper gastrointestinal bleeding due to pancreatic pseudocyst rupture into the duodenum, which developed during anticoagulation therapy for acute pancreatitis associated with portal vein thrombosis has been reported [18]. Thus bleeding risk on anticoagulation needs to be monitored closely in these patients. Our study shows that over five years' period, treatment of PVTT with anticoagulation, there is not much benefit in anticoagulation therapy with increase in bleeding risk in these patients. The overall improvement in mortality rates is indicative of effective treatment in patients. These future studies may help shape future guidelines of management of patients with PVTT, and improve patient mortality rates, survival duration, and overall outcomes.

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