Post-PCI antiplatelet therapy in patients with liver cirrhosis

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Post-PCI antiplatelet therapy in patients with liver cirrhosis

• Case scenario
• CHD in patients with hepatic cirrhosis
• PCI in patients with hepatic cirrhosis
• Ischemic risk in patients with hepatic cirrhosis
• Bleeding risk in patients with hepatic cirrhosis
• Conclusion

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• Case scenario
Clinical data

- Male, m m a a
- 62 y
- Type 2 DM, HTN
- Class III AP despite OMT
- SVD, mid-LAD 80% lesion
- No history of GIT bleeding
- No esophageal varices
- Platelets count 70 000
- Prepared for liver transplantatin
Treatment strategy

- There is no information in the literature about the outcomes of PCI in patients with CAD and ESLD.
- However, it has been suggested that symptomatic, medically refractory angina in liver transplantation candidates should be treated with PCI (preferably BMS and limited dual antiplatelet therapy).

PCI and stenting

28 June 2015:
- Lesion: mid LAD 80% focal calcified
- Guiding: XB 3.5 6F
- Wire: BMW 0.014 floppy
- Stent: 3.5 28 vision (BMS) (Abbot)
- Technique: direct stenting at 20 atm
Clinical course

- Stable
- Discharged on same day
- Usual treatment including DAP
  - 2-days latter patient developed massive hematuria
  - Modified dose of DAP: low-dose ASA and clopidogril given every other day
  - Completely asymptomatic

Last follow-up 20 Feb. 2017

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HCV is a major endemic medical health problem in Egypt

- 14.7% of the population are infected
- The highest prevalence in any population in the world.
- Nile Delta and Upper Egypt, infection rates can be much higher at around 26% and 28%
- HCV seroprevalence up to 40% in some areas of Egypt based on blood-bank surveys
- 170,000 new cases every year to add to the
- 11.5 million patients suffering from the disease
HCV infection and ischaemic heart disease

Table 3. Main studies assessing the association between hepatitis C virus (HCV) infection and ischaemic heart disease.

<table>
<thead>
<tr>
<th>References, year</th>
<th>Type of study</th>
<th>Country</th>
<th>HCV+ (n)</th>
<th>HCV− (n)</th>
<th>Statistics</th>
<th>Diagnosis method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies showing an association</td>
<td></td>
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<tr>
<td>Vasauline et al. (11), 2004</td>
<td>Cross-over</td>
<td>Italy</td>
<td>491</td>
<td>195</td>
<td>OR = 4.295% CI: 1.4-13</td>
<td>HCV antibody</td>
</tr>
<tr>
<td>Alyan et al. (40), 2008</td>
<td>Cross-sectional</td>
<td>Turkey</td>
<td>139</td>
<td>225</td>
<td>OR = 2.02 95% CI: 1.58-2.58</td>
<td>HCV antibody</td>
</tr>
<tr>
<td>Butt et al. (36), 2009</td>
<td>Cross-sectional</td>
<td>USA</td>
<td>82 063</td>
<td>89 582</td>
<td>HR = 1.25 95% CI: 1.2-1.3</td>
<td>ICD-9</td>
</tr>
<tr>
<td>Tsui et al. (35), 2009</td>
<td>Cross-sectional</td>
<td>USA</td>
<td>84</td>
<td>897</td>
<td>HR = 2.13 95% CI: 1.19-3.80</td>
<td>HCV antibody</td>
</tr>
<tr>
<td>Rambohn et al. (45), 2010</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>78</td>
<td>–</td>
<td>OR = NA</td>
<td>HCV antibody</td>
</tr>
<tr>
<td>Freberg et al. (41), 2011</td>
<td>Cross-sectional**</td>
<td>USA</td>
<td>1439</td>
<td>5453 (HIV−)</td>
<td>HR = 2.03 95% CI: 1.28-3.21</td>
<td>ICD-9</td>
</tr>
<tr>
<td>Studies not showing an association</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Vosiek et al. (50), 2004</td>
<td>Transversal</td>
<td>Germany</td>
<td>21</td>
<td>4033</td>
<td>OR = NA</td>
<td>HCV antibody</td>
</tr>
<tr>
<td>Butt et al. (42), 2007</td>
<td>Cross-sectional</td>
<td>UK</td>
<td>126 926</td>
<td>126 926</td>
<td>OR = NA</td>
<td>ICD-9</td>
</tr>
<tr>
<td>Forde et al. (37), 2012</td>
<td>Retrospective cohort</td>
<td>USA</td>
<td>4909</td>
<td>71 668</td>
<td>HR = 1.1 95% CI: 0.67-1.83</td>
<td>ICD-9</td>
</tr>
<tr>
<td>Ounissi et al. (34), 2013</td>
<td>Cross-sectional</td>
<td>USA</td>
<td>173</td>
<td>19568</td>
<td>OR = NA</td>
<td>HCV RNA</td>
</tr>
</tbody>
</table>

**HIV patients; HR, hazard ratio; ICD-9, International Classification of Diseases-9; NA, not available; OR, odds ratio; 95% CI, 95% confidence interval.

CardioAlex 2013 Abstracts

Patients and methods: This study group included two groups of patients, with angiographically documented CAD: 25 HCV seropositive patients as test group and another 25 HCV seronegative patients as control group. Both groups were comparable as regard, age, sex, hypertension, and diabetes mellitus, and smoking. A detailed qualitative coronary angiographic analysis and SYNTAX score were used to assess the extent and severity of CAD.

Results: The presence of total occlusion was significantly higher in the HCV seropositive group (p < 0.05) and the SYNTAX score was higher (14.86 ± 6.64 vs. 10.86 ± 7.28, p < 0.05). After adjustment, HCV seropositivity still represented an independent predictor for severity of coronary atherosclerosis demonstrated by higher SYNTAX score (p < 0.05).

Conclusion: HCV infection is an independent predictor for severe coronary atherosclerosis, as demonstrated by higher syntax score. It also associated with higher incidence of totally occluded coronaries.

Hepatitis C Virus (HCV) Infection as a novel risk factor for severe coronary artery disease: A Prospective Angiographic Study


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Chronic hepatitis C virus infection, a new cardiovascular risk factor?

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Figure 1: Possible mechanisms connecting HCV infection and cardiovascular disease. HCV is considered a "metabolic" virus and is associated with metabolic disorders, in particular insulin resistance and type 2 diabetes mellitus, which are proatherogenic conditions. By inducing hepatic injury and activating peripheral blood mononuclear cells (PBMC), HCV increases circulating levels of proinflammatory cytokines, leading to peripheral IR and hyperinsulinemia. Furthermore, a key feature of HCV infection is associated with hyperhomocysteinaemia, hyperadiponectinaemia, oxidative stress, lipid peroxidation, and all components of the metabolic syndrome. Therefore, "viral" induced and "metabolic" steatosis, together with the direct stimulus of increased insulin levels on hepatic stellate cells (HSC), likely stimulate the progression of fibrosis within the liver parenchyma. Furthermore, systemic inflammation, the procoagulant state, and direct viral effects on the vascular wall may contribute to the development and progression of the atherogenic process.
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PCI in patients with CAD and ESLD

- There is no information in the literature about the outcomes of PCI in patients with CAD and ESLD.
- However, it has been suggested that symptomatic, medically refractory angina in liver transplantation candidates should be treated with PCI (preferably BMS and limited dual antiplatelet therapy).

Antiplatelets post-PCI in patients with hepatic cirrhosis

- The currently available evidence suggests that low-dose aspirin is relatively safe in terms of bleeding risk in patients with cirrhosis, but without significant varices after coronary artery stenting.

(Lisman et al. J of Hepatology. 2013; 59, 358)
Antiplatelets post-PCI in patients with hepatic cirrhosis

- The pharmacokinetics and pharmacodynamics of Clopidogrel are unaltered in patients with Child A or B cirrhosis
- A major disadvantage of the clopidogril is that they require metabolic activation by the liver
- Reversible P2Y12 inhibitor Ticagrelor does not require metabolic activation, but is cleared by the liver
- (Lisman et al. J of Hepatology. 2013; 59, 358)

Antiplatelets post-PCI in patients with hepatic cirrhosis

- The use of P2Y12 inhibitors for prevention of arterial events in cirrhosis may be limited to those patients without varices, since the rate of variceal bleeding in patients receiving antiplatelet agents following stent placement was substantial (12.5%)

(Lisman et al. J of Hepatology. 2013; 59, 358)
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Factors favoring prothrombotic state

- Increased synthesis of factor 8
- Increased levels of von-Willebrand factor
- Decreased liver synthesis of protein C, protein S and anti-thrombin 3
- Genetic predisposition such as factor 5 Leiden

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DOI: 10.1159/000442877

Khoury/Ayman/Cohen/Daher/Shmuel/Mizrahi
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Factors favoring anticoagulant state

- Decreased synthesis of coagulation factors (II, V, VII, X, XI, XII, XIII) and fibrinogen
- Reduced clearance of tissue plasminogen activator
- Thrombocytopenia
- Impaired platelets function
- Vitamin K deficiency

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CONCLUSION

- ESLD due to chronic HCV infection is a major health problem in EGYPT
- CHD is frequently seen in patients with hepatic cirrhosis
- Revascularization using BMS in selected patients is an option for cirrhotic patients peppered for LT
- DAP can used safely after coronary stenting in patients with CHD and liver cirrhosis child A and B
- Esophageal varies is a contraindication for the use of DAP and should be treated first before revascularization
- Clinician should balance between thrombotic and bleeding risk in patients with CHD and ESLD
Thank You