Heart transplant recipients with cardiac allograft vasculopathy have increased platelet aggregation before and after low-dose aspirin therapy

Authors:
KP Bjerre¹, TS Clemmensen¹, K Berg¹, SH Poulsen¹, S Dalby¹, AM Hvas¹, EL Grove¹, H Eiskjaer¹, ¹Skejby University Hospital - Aarhus - Denmark,

Topic(s):
Coronary Artery Disease: Pharmacotherapy

Citation:
Aarhus University (PhD-salary)

BACKGROUND
Following heart transplantation (HTx), long-term survival is reduced mainly due to development of a specific form of coronary artery disease, coronary allograft vasculopathy (CAV). Using optical coherence tomography to visualize the coronary artery wall, we have recently shown that layered fibrotic plaques resembling organized clots are the dominant plaque component in CAV. Thus, thrombosis is suggested as a possible mechanism contributing to development and progression of CAV. Aspirin is widely used after HTx despite limited evidence and lack of specific guidelines. The antiplatelet effect of aspirin has not been thoroughly examined in HTx-patients.

PURPOSE
To investigate baseline platelet aggregation and the antiplatelet effect of aspirin in HTx-patients with and without CAV.

METHODS
We included 68 HTx-patients (median 8.6 years from HTx). In 66 patients taking 75 mg aspirin for a minimum of 7 days, platelet aggregation was measured in whole blood using impedance aggregometry with the following agonists: Adenosine diphosphate (ADP) stimulating ADP-receptors and arachidonic acid (AA) for monitoring of aspirin treatment. Aspirin compliance was confirmed by measuring serum-thromboxane B2. Platelet aggregation prior to aspirin therapy was measured in 59 patients as it was not considered clinically safe to interrupt ongoing aspirin treatment for one week prior to blood sampling in 9 patients mainly due to previous coronary stenting. CAV burden was determined by coronary angiography and echocardiography based on international classification. Patients were divided into two groups; no CAV (n=37) and CAV (n=29).

RESULTS
In HTx-patients not treated with aspirin, we found significantly increased ADP-induced platelet aggregation in patients with CAV vs. patients without CAV (904 (95% CI 813-995) vs. 786 (95% CI 728-843) AU*min, P=0.02). Baseline AA-induced aggregation was also higher in patients with CAV vs. patients without CAV, though non-significant (994 (95% CI 907-1081) vs. 905 (95% CI 839-972) AU*min, P=0.10). Even though aspirin reduced AA-induced platelet aggregation in both groups, patients with CAV had significantly increased AA-induced platelet aggregation compared with patients without CAV on aspirin treatment (380 (95% CI 295-465) vs. 286 (95% CI 239-334) AU*min, P=0.04) (Fig. 1).

CONCLUSIONS
HTx-patients with CAV have increased platelet aggregation before and after aspirin treatment compared with HTx-patients without CAV. Aspirin monotherapy may not provide sufficient platelet inhibition in HTx-patients with CAV.
Heart transplant recipients with cardiac allograft vasculopathy have increased platelet aggregation before and after low-dose aspirin therapy.

Authors:
KP Bjerre, TS Clemmensen, K Berg, SH Poulsen, S Dalby, AM Hvas, EL Grove, H Eiskjaer

1 Skejby University Hospital – Aarhus – Denmark,

Topic(s): Coronary Artery Disease: Pharmacotherapy

BACKGROUND
Following heart transplantation (HTx), long-term survival is reduced mainly due to development of a specific form of coronary artery disease, coronary allograft vasculopathy (CAV). Using optical coherence tomography to visualize the coronary artery wall, we have recently shown that layered fibrotic plaques resembling organized clots are the dominant plaque component in CAV. Thus, thrombosis is suggested as a possible mechanism contributing to development and progression of CAV. Aspirin is widely used after HTx despite limited evidence and lack of specific guidelines. The antiplatelet effect of aspirin has not been thoroughly examined in HTx-patients.

PURPOSE
To investigate baseline platelet aggregation and the antiplatelet effect of aspirin in HTx-patients with and without CAV.

METHODS
We included 68 HTx-patients (median 8.6 years from HTx). In 66 patients taking 75 mg aspirin for a minimum of 7 days, platelet aggregation was measured in whole blood using impedance aggregometry with the following agonists: Adenosine diphosphate (ADP) stimulating ADP-receptors and arachidonic acid (AA) for monitoring of aspirin treatment. Aspirin compliance was confirmed by measuring serum-thromboxane B2. Platelet aggregation prior to aspirin therapy was measured in 59 patients as it was not considered clinically safe to interrupt ongoing aspirin treatment for one week prior to blood sampling in 9 patients mainly due to previous coronary stenting. CAV burden was determined by coronary angiography and echocardiography based on international classification. Patients were divided into two groups; no CAV (n=37) and CAV (n=29).

RESULTS
In HTx-patients not treated with aspirin, we found significantly increased ADP-induced platelet aggregation in patients with CAV vs. patients without CAV (904 (95% CI 813–995) vs. 786 (95% CI 728–843) AU*min, P=0.02). Baseline AA-induced aggregation was also higher in patients with CAV vs. patients without CAV, though non-significant (994 (95% CI 907–1081) vs. 905 (95% CI 839–972) AU*min, P=0.10). Even though aspirin reduced AA-induced platelet aggregation in both groups, patients with CAV had significantly increased AA-induced platelet aggregation compared with patients without CAV on aspirin treatment (380 (95% CI 295–465) vs. 286 (95% CI 239–334) AU*min, P=0.04) (Fig. 1).

CONCLUSIONS
HTx-patients with CAV have increased platelet aggregation before and after aspirin treatment compared with HTx-patients without CAV. Aspirin monotherapy may not provide sufficient platelet inhibition in HTx-patients with CAV.

Fig. 1. Arachidonic acid-induced platelet aggregation before aspirin therapy and after a minimum of 7 days of aspirin therapy in heart transplant recipients with and without cardiac allograft vasculopathy (CAV).