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Review Article

Cardiac evaluation of haemodialysis-related hypotension using dobutamine stress echocardiography

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SUMMARY: Haemodialysis-related hypotension occurs in approximately 30% of patients. Myocardial ischaemia and/or insufficient contractile reserve in response to sympathetic stress may be involved in the pathogenesis of hypotension during dialysis. Using dobutamine stress echocardiography, left ventricular function at rest, myocardial contractile reserve and the presence and extent of ischaemia can be assessed in a non-invasive way. This short review will focus on the potential value of dobutamine stress echocardiography for the evaluation of hypotension-prone haemodialysis patients.

KEY WORDS: **dobutamine stress echocardiography, intradialytic hypotension, myocardial contractile reserve.**

INTRODUCTION

Cardiovascular disease occurs frequently in patients with end-stage renal failure and is by far the main cause of death in these patients.[1] In addition to classical cardiovascular risk factors such as hypertension and hyperlipidaemia, hyperhomocysteinaemia, endothelial dysfunction and increased oxidative stress have been identified as important additional risk factors in patients with end-stage renal disease.[1,2]

Hypotension during haemodialysis is a frequently encountered clinical problem and has been reported to occur in 20–50% of all patients on chronic haemodialysis.[3–6] The pathophysiology of haemodialysis-induced hypotension is complex and multifactorial.[6] Factors involved are both patient-related (such as underlying coronary artery disease), left ventricular (LV) diastolic and systolic dysfunction, autonomic nervous system dysfunction and haemodialysis-related factors such as speed and amount of ultrafiltration and the type and temperature of the dialysate used.[1,6,7]

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DOBUTAMINE STRESS ECHOCARDIOGRAPHY (DSE)

With DSE it is possible to assess LV function at rest and the presence of coronary artery disease in a non-invasive way.[8] According to the guidelines of the American Society of Echocardiography, the LV is subdivided into 16 segments.[9] Each segment is evaluated for its wall motion and thickening, both at rest and during DSE, using a five-point score (normokinesia, mild hypokinesia, severe hypokinesia, akinesia and dyskinesia). In addition to systolic function, diastolic function can be evaluated using Doppler flow measurements of early diastolic (E wave) and late diastolic filling waves (A wave) across the mitral valve and time intervals (isovolumetric contraction and relaxation time).

At lower infusion rates (10 μg/kg/min) dobutamine predominantly exerts an inotropic effect, whereas at higher infusion rates the chronotropic effect prevails. Hence, with the lower infusion rates information about myocardial contractile reserve is obtained, while at higher infusion rates information about the presence of ischaemia is obtained. Ischaemia is detected by DSE as new wall motion abnormalities.

The accuracy of DSE in diagnosing coronary artery disease has been confirmed in a large number of patients, including patients with end-stage renal disease with significant coronary artery disease as diagnosed by coronary angiography.[10,11] Hypotension and cardiac arrhythmias are the most frequently occurring side-effects of DSE.

The overall incidence of these side-effects is low, varying between 2% and 3%,[12] and appears not to be related to the induction of ischaemia. Although reports are scarce, adverse effects may occur more frequently in patients with end-stage renal disease requiring haemodialysis. In a reported study performed on haemodialysis patients, DSE-induced hypotension (decrease in systolic blood pressure >40 mmHg) occurred in 6 out of 36 patients (16%).[13] In another study, atrial fibrillation was reported to occur 5–10 times more often in haemodialysis than in non-haemodialysis patients. The advice is therefore to perform DSE prior to, not after, a haemodialysis session when the patient is in a relatively hypervolaemic condition.

Anti-anginal therapy, especially beta-blockers, is usually skipped on the morning of the test and continued after the test. Beta-blockers shift the heart rate dobutamine-response curve to the right, and contractile reserve may be elicited only at a higher dobutamine plasma level compared with patients without beta-blockers. The evaluation of contractile reserve is not influenced by beta-blockers provided that a prolonged low-dose dobutamine infusion protocol is used. Compared with the standard 3-min interval dose steps, increasing dobutamine infusion dose with 10 μg/kg/min up to 40 μg/kg/min, the prolonged low-dose dobutamine infusion protocol has a 5 μg/kg/min infusion rate for 5 min and a 10 μg/kg/min for 5 min. Thus, this protocol induces a more reproducible and higher dobutamine plasma level at the end of the low-dose (10 μg/kg/min) infusion stage. For those patients not achieving target heart rate at the end of the test, atropine is added. Furthermore, care must be taken to ensure that electrolyte abnormalities have been corrected before the test is performed.

Stroke volume during DSE can be calculated from apical two- and four-chamber views using a modification of Simpson's rule. The principle of the Simpson's rule is to divide the LV volume into slices of known thickness. The volume of the LV is then equal to the sum of the volumes of the slices. Stroke volume is assessed by the difference between end-diastolic and end-systolic volume.[9]

In a recent study[13] we applied DSE to evaluate cardiac contractile reserve and the presence of myocardial ischaemia in hypertension-prone (HP) and hypertension-resistant (HR) haemodialysis patients, matched for volume status, cardiac risk factors and duration of haemodialysis (Table 1). Dobutamine-induced ischaemia, as defined by new wall motion abnormalities, was observed in only three of the HR and four of the HP patients. However, compared with the HR patients, myocardial contractile reserve (increase in stroke index in response to dobutamine) was impaired in a considerably larger proportion of the HP than HR patients. As a consequence of this reduced myocardial contractile reserve, the dobutamine-induced maximal increase in cardiac index was considerably lower in the HP patients.

Table 1 Results of dobutamine stress echocardiography in hypotension-prone (HP) and hypotension-resistant (HR) haemodialysis patients

	HR ($n=11$)	HP ($n=11$)	*P*-value
Medication			
Beta-blockers	12	6	0.04
Angiotensin-converting enzyme inhibitors	9	5	NS
Noradrenaline (pg/mL)	429 ± 209	381 ± 174	NS
Ischaemia induced during DSE	4	3	1.0
Hypotension during DSE	2	4	0.4
Stroke index (ml/m^2)			
Rest	39 ± 9	33 ± 9	
Low-dose dobutamine	41 ± 12	31 ± 9	< 0.01
Peak dobutamine stress	36 ± 13	26 ± 10	< 0.01

Variables are expressed as mean values ± SD. DSE, dobutamine stress echocardiography. Hypotension during DSE is a decrease of systolic blood pressure > 40 mmHg. Stroke index is stroke volume corrected for body surface area and expressed as ml/m^2. Calculation of the stroke volume is detailed in the text.

When translating the results of DSE to the clinical situation, we suggest that the inability of the cardiac index to increase in response to sympathetic stress can play a key role in the pathogenesis of haemodialysis-induced hypotension. If haemodialysis-induced activation of the sympathetic nervous system does not lead to an appropriate rise in cardiac output to maintain blood pressure, further sympathetic discharge is likely to occur. Eventually, owing to exhaustion, the autonomic nervous system is no longer capable of maintaining this high level of sympathetic tone and blood pressure will fall. The cause of haemodialysis-induced hypotension in this situation is not primarily a consequence of failure of the autonomic nervous system but the consequence of diminished myocardial responsiveness or myocardial contractile reserve.

Although DSE can evoke hypotension in haemodialysis patients, there is also limited evidence that infusion of dobutamine during haemodialysis can actually reduce the number of hypotensive episodes.[14] Possibly, this may be related to recruitment of contractile reserve by dobutamine.

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