



# Dobutamine Stress Echocardiography in the Diagnosis of Asymptomatic Ischemic Heart Disease in Patients With Chronic Kidney Disease—Review of Literature and Single-Center Experience

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## ABSTRACT

**Background.** Coronary artery disease (CAD) may be present in kidney transplant (KT) candidates without the presence of CAD clinical symptoms. This study joins an ongoing discussion about appropriate noninvasive diagnostic approaches for ischemic heart disease (IHD) assessment and patient selection for revascularization procedures. The aim of this study was to evaluate the role of dobutamine stress echocardiography (DSE) in IHD diagnosis in initially asymptomatic maintenance hemodialysis (HD) patients.

**Methods.** Forty HD patients aged  $52.4 \pm 2.0$  years, were studied for 2.5 years. At inclusion, they were free of both symptoms and history of IHD. Standard electrocardiography (ECG), chest X-ray, standard echocardiography, DSE, 24-hour Holter ECG, and Doppler ultrasonography (carotids and lower extremities) were performed. Results were analyzed according to a predefined diagnostic algorithm.

**Results.** DSE yielded negative results in all patients. Left ventricular (LV) ejection fraction  $\leq 60\%$ , LV hypertrophy, and Holter ECG silent ischemia features were noticed in 15%, 70%, and 10% of patients, respectively. Atherosclerotic lesions in lower extremities and carotid arteries were present in 50% and 37.5% of patients, respectively. During the follow-up, 9/40 patients died, including 6 cardiovascular (CV) deaths: 2 with intermediate and 4 with high CV risk according to the proposed algorithm.

**Conclusions.** In asymptomatic KT candidates, not only DSE, but also other noninvasive tests (eg, echocardiography and Doppler ultrasonography of the carotid and peripheral arteries) along with a detailed profile of the remaining CV risk factors should be performed and analyzed. Defined composition of risk factors and particular changes in noninvasive tests may be an indication for coronary angiography.

**T**HE PRESENCE of classic and chronic kidney disease (CKD)-specific risk factors for ischemic heart disease (IHD) [1] renders CKD patients as a population at high risk for cardiovascular (CV) complications and sudden cardiac death [2–4]. CKD also predisposes the patient to developing autonomic neuropathy involving cardiac and vascular innervation [5–8]. Altered mechanisms of angina perception may be one of the consequences, and indeed, asymptomatic

IHD is a predominant form of IHD (up to 75%) in this patient population [9].

In outpatient kidney clinics and dialysis facilities, the selection process for kidney transplantation (KT) frequently

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involves asymptomatic high-CV-risk CKD patients. Noncardiac surgery such as KT is typically related to a degree of risk for CV complications for the recipient. American cardiovascular societies (American College of Cardiology [ACC]/American Heart Association [AHA]), however, do not recommend routine screening for the “low-risk” asymptomatic population of KT candidates. Therefore, the question arises concerning the “low-risk” CKD patient definition. As already mentioned [2–4,9], all CKD patients are unequivocally considered to be at an increased risk, with their CV status equivalent to that of diabetic patients without CKD. An appropriate noninvasive diagnostic approach to screening asymptomatic KT candidates for the presence of IHD is an additional problem. The issues described above clearly point to an urgent necessity for the development of a universal and uniform diagnostic algorithm that would provide a safe “diagnostic sieve” to prevent post-KT CV events. On the other hand, care should be taken to avoid adoption of too strict selection criteria that would unnecessarily defer the decision regarding KT in, or disqualify, potential recipients who might otherwise benefit from the procedure. Finally, the question arises of what the best management strategy is for patients with coronary artery stenoses identified in the course of the diagnostic workup, ie, which patients should be treated interventionally and which patients would benefit from conservative treatment. Last but not least, there is the question of what impact these strategies might have on another chance for KT. These unresolved questions have been on the agenda at numerous meetings of leading working groups of European and international societies for the past 10 years [10].

In high-risk patients in whom noncardiac surgery is planned, ACC/AHA recommend noninvasive stress testing to assess CV risk. These tests include treadmill exercise, dobutamine stress echocardiography (DSE), dipyridamole stress echocardiography, and single-photon-emission computerized tomography with dipyridamole [11]. However, the DECREASE II study did not demonstrate the postoperative benefits of such preventive measures and incited concern among experts as to whether this noninvasive strategy would not result in KT delay. The usefulness of cardiac noninvasive stress testing before noncardiac surgery was studied by Wijeyesundera et al in a retrospective cohort study in Ontario, Canada [12]. In 8.9% of the studied patients, stress tests were performed before surgery: exercise treadmill stress test, exercise or dobutamine stress echocardiography, or perfusion scintigraphy with exercise or dipyridamole infusion. End points included 1-year postoperative mortality and length of hospital stay. The meta-analysis demonstrated that noninvasive stress testing is a justified strategy in patients with intermediate or high risk of postoperative CV complications (ie, patients with  $\geq 1$  risk factor, such as IHD, diabetes, chronic heart failure [CHF], carotid artery disease, or CKD). Thus, data from studies concerning this issue are unequivocal, expert consensus is currently lacking, and no larger multicenter studies on the population of CKD patients have been carried out that might provide reliable algorithms for preoperative management.

DSE has been proposed among stress tests recommended for this patient population [13,14]. This modality was expected to serve as a universal diagnostic tool for noninvasive IHD detection in CKD patients, because a pharmacologic stressor (dobutamine) is used instead of physical exercise. DSE is currently the most commonly used type of stress test [15,16]. Indications for DSE are summarized in Table 1 [14,16]. Most common indications include a patient’s inability to exercise and electrocardiography (ECG) alterations at rest rendering exercise ECG interpretation difficult. DSE can also be used in patient groups where high false positive rates can be expected: asymptomatic patients with diabetes, CKD, and peripheral artery disease (PAD) [15,17]. Its sensitivity and specificity for IHD detection are quite satisfactory (76%–92% and 72%–89%, respectively) [17,18]. Taking into account that IHD detection in CKD patients can be challenging (eg, atypical, uninterpretable ECG tracing, alterations in radiotracer distribution on scintigraphy, inability to achieve target rate during exercise testing owing to comorbidities), DSE seems to be a valuable alternative among all the noninvasive tests [12,14–16,18,19]. However, high false negative rates of DSE in CKD patients have been reported. Therefore, the question of whether DSE is an appropriate diagnostic modality in CKD patients remains unresolved. In the present paper, we present the results obtained by our team, including a 10-year analysis of this issue, and prospective follow-up results. Our results are discussed in the context of expert opinions published in the literature.

The aim of this study was to assess the usefulness of DSE for IHD diagnosis in asymptomatic patients receiving hemodialysis (HD) and to place that in the context of available literature concerning this controversial issue.

## MATERIAL AND METHODS

### Inclusion Criteria

Forty patients receiving chronic HD (aged  $52.4 \pm 2.0$  years) in the Dialysis Facility of the Provincial Specialist Hospital in Olsztyn, Poland, were examined. Time on dialysis at inclusion ranged from 4 months to 23 years (average  $5.21 \pm 0.85$  years). All patients were prospectively followed for 2.5 years. Exclusion criteria included clinical symptoms or history of IHD and history of stroke or transient ischemic attack (TIA). Other exclusion criteria included infection, active bleeding, neoplasm, or mental disorders precluding patient cooperation.

### Cardiovascular Diagnostic Workup

Cardiovascular diagnostic workup included standard 12-lead ECG, chest X-ray, echocardiography, DSE, 24-hour Holter ECG recording, and duplex ultrasonography of the carotid and peripheral arteries. These tests were performed before the middle HD session of the HD cycle of 3 sessions per week, 1 session every other day. Cardiovascular work-up was performed in the Department of Cardiology and duplex ultrasonography assessment of peripheral arteries in the Ultrasonography Laboratory of the Provincial Specialist Hospital in Olsztyn.

Echocardiography was performed with the use of a GE-Vingmed System 5 echocardiographic device equipped with a 2.5–3.5-MHz transducer. The following M-mode parameters were measured: left

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