

## Interest of the SUDOSCAN in the screening of cardiac autonomic neuropathy in type 2 diabetics

Fatima Zahra. El Jaafari \*, Widad. Douali, Sana. Rafi, Ghizlane. El Mghari and Nawal. El Ansari

*Department of endocrinology, diabetology, metabolic diseases and nutrition CHU Mohamed VI Marrakech, Morocco.*

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### Abstract

**Introduction:** Cardiac autonomic neuropathy (CAN) is one of the first complications of type 2 diabetes (T2DM) and a silent cause of cardiovascular morbidity and mortality. SUDOSCAN, a digital chronoamperometric analysis device, has appeared in recent years and allows a rapid and non-invasive quantitative assessment of sudomotor function, which will allow the measurement of sympathetic cholinergic function in the assessment of CAN by reflecting the state of the autonomic nervous system.

The main purpose of the present study is to evaluate the usefulness of SUDOSCAN in the detection of cardiac autonomic neuropathy in type 2 diabetic patients.

**Patients and methods:** In this study we recruited 85 patients with type 2 diabetes. The study data were collected by questionnaire, clinical examination and SUDOSCAN.

**Results:** The 85 patients had a mean age of  $58.32 \pm 10.89$  years, with a large female predominance, and a sex ratio of 0.28. 67% of our patients had diabetes for less than 10 years. The SUDOSCAN measurement noted 54.1% with a moderate risk of having CAN, 45.9% with a low risk, and a zero percentage with a high risk of having CAN.

**Conclusion:** The risk score for cardiac autonomic neuropathy assessed by SUDOSCAN, and its ease of use and interpretation, make it a good screening test for cardiac autonomic neuropathy in patients with type 2 diabetes.

**Keywords:** Type 2 diabetes; Diabetic cardiac autonomic neuropathy; Autonomic nervous system; SUDOSCAN; Sudomotor function; Sweat electrical conduction; Electrocardiogram

### 1. Introduction

Cardiac autonomic neuropathy (CAN) is one of the first complications of type 2 diabetes (T2DM) and a silent cause of cardiovascular morbidity and mortality. CAN is present in 90% of patients with type 1 diabetes and 20-73% of patients with type 2 diabetes [1]. It reflects dysfunction of the autonomic nervous system (ANS) and regulation of the cardiovascular system. The ANS is the main extrinsic control mechanism that regulates heart rate, blood pressure and myocardial contractility [2,4]. Sudomotor dysfunction is one of the earliest findings in distal small fiber neuropathy and correlates closely with the presence of CAN [1,2].

A digital chronoamperometric analysis device (SUDOSCAN) has emerged in recent years, which allows a rapid and non-invasive quantitative assessment of sudomotor function. The device measures the electrochemical conductance of the

\* Corresponding author: F Z. El Jaafari

skin, which results from the electrochemical reaction between the sweat chlorides and the electrodes in contact with the hands and feet [2,3].

The assessment of sudomotor function provides a measure of sympathetic cholinergic function as part of the ASC workup by reflecting the state of the autonomic nervous system [4].

The main aim of the present study is to evaluate the usefulness of the SUDOSCAN in screening for cardiac autonomic neuropathy in type 2 diabetic patients.

## 2. Material and methods

This is a prospective cross-sectional and descriptive study of 85 patients with type 2 diabetes followed at the Department of Endocrinology, Diabetology and Metabolic Diseases of the Mohammed VI University Hospital of Marrakech.

Information on the socio-demographic data of the participants, their medical history, the duration of diabetes and its treatment, and associated complications were collected during an interview using a previously established questionnaire.

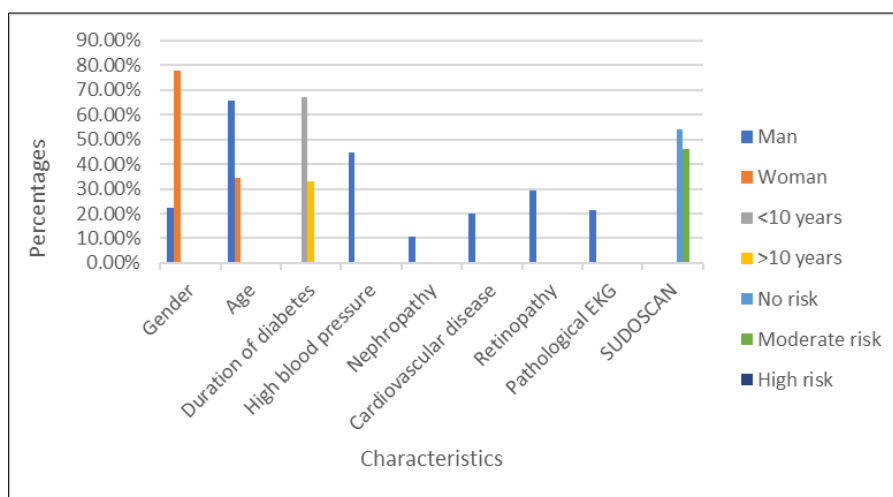
Clinical examination and various clinical parameters were performed and specified such as: weight and height, BMI, blood pressure, EKG and GPI.

SUDOSCAN, a unique, simple and non-invasive device, was performed on our patients, which is able to detect and monitor small fiber neuropathies that are usually not detected by traditional tools. It consists of a computer and 4 electrodes on which patients place their bare hands and feet. In less than 3 minutes, it provides stimulation of the sweat glands which assesses small nerve fibers (C-fibers) [5]. This early detection improves the management of the disease and prevents serious complications.

Patients were classified according to the values of the electrochemical conductance of the feet (CECP, expressed in micro-Siemens,  $\mu\text{S}$ ) into no-risk ( $\text{CECP} > 60 \mu\text{S}$ ), moderate-risk ( $40\text{-}60 \mu\text{S}$ ) or high-risk ( $< 40 \mu\text{S}$ ) subjects, these cut-off values were defined based on previous studies [5,6].

Our data were entered using Microsoft Office Word 2019. Statistical analysis was performed using Microsoft Office Excel 2019.

## 3. Results



**Figure 1** Epidemiological, clinical and paraclinical characteristics of our series

Our series included 85 type 2 diabetic patients, we noted a large female predominance, with a sex ratio of 0.28.

A large proportion (67%) of our population had suffered from diabetes for less than 10 years, and only 21.4% of the participants had a pathological EKG. We also noted in the SUDOSCAN results that the majority of patients (54.1%) had a moderate risk of having an ASC, 45.9% had a low risk, while the percentage of a high risk of having an ASC was zero. (Fig1)

#### 4. Discussion

Cardiac autonomic neuropathy (CAN) associated with diabetes damages the autonomic nerve fibers that innervate the heart and blood vessels, resulting in abnormalities of heart rhythm and vascular dynamics. It affects several systems and is a major cause of morbidity and mortality in patients with diabetes [13].

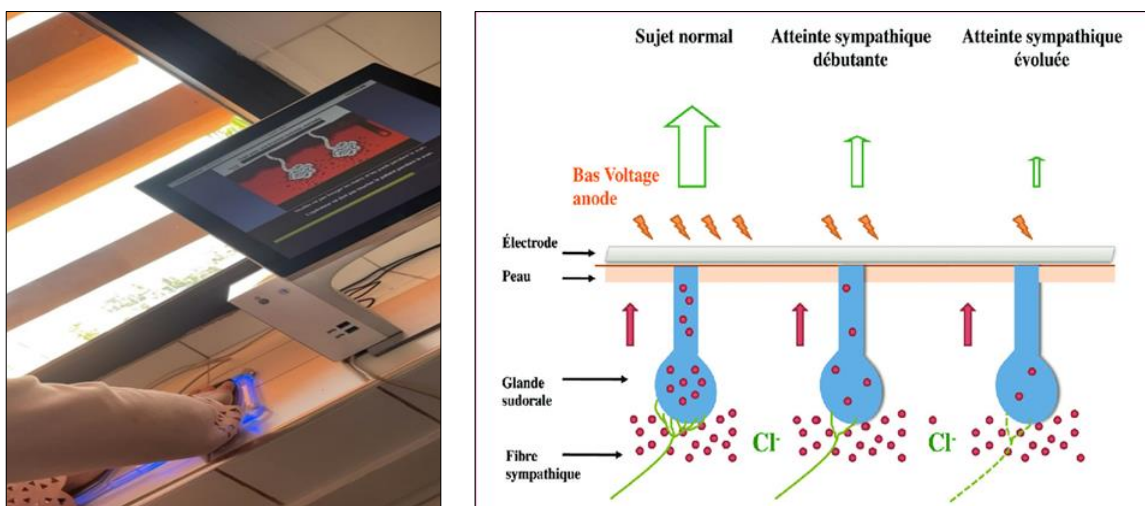
Learned societies recommend screening for ANC in patients with T2DM at first diagnosis, whereas in T1DM, screening takes place five years after disease onset [11]. Dysglycemia is not the only cause of CAD onset and progression in T2DM, obesity and associated dyslipidemia, hyperinsulinemia and hypertension are additional risk factors for CAD in T2DM [10,12]. Thus, it appears that different etiological factors of diabetes contribute differentially to the manifestations of CAN [10].

Of the different functional subsystems of the ANS, the cardiovascular autonomic nervous system is most often examined using parameters such as heart rate and blood pressure. Sudomotor testing is a useful adjunct to the assessment of the cardiovascular autonomic nervous system, as impaired neurogenic sweating is one of the first clinical signs of various autonomic neuropathies, as well as neurodegenerative disorders, and significantly reduces quality of life. Clinically In the first instance, the autonomic nervous system is assessed with a detailed history of autonomic function and a general clinical examination [5].

SUDOSCAN is a new technique that uses reverse iontophoresis and chronoamperometry to assess the chloride ion concentration of the skin as a measure of sudomotor production. The applied electric current induces a shift of chloride ions from the sweat glands to the outer skin surface, resulting in a current between the anode and a reference electrode that is proportional to the skin chloride concentration. This technique is easy to implement and has been studied in patients with diabetic neuropathy [7].

Sweat glands are innervated by small amyelinated fibers, and exploration of sweat function has been proposed to assess the severity of autonomic nervous system damage [3,14]. The American Diabetes Association (ADA) suggests that measurement of sweat function should be included in the tests used to screen for and diagnose diabetic neuropathies [3,15]. The Toronto Expert Consensus also advocates the use of this test for the early detection of autonomic nervous system damage [3, 15].

SUDOSCAN risk scores are automatically calculated from electrochemical skin conductivity values, BMI and age, using an algorithm included in the device software. The scores are presented as percentages, and higher risk scores are associated with an increased risk of autonomic heart defects [4,16].



**Figure 2** Principle and electrochemical mechanism of the SUDOSCAN

Due to the complexity of the autonomic nervous system, many phenomena have not yet been elucidated, so that autonomic functional diagnosis is in constant evolution.

Although less established and less widely used than cardiovascular autonomic testing, the assessment of sudomotor function is of increasing interest both for research studies and for clinical diagnostic evaluation. In addition, studies have shown that neurogenic sweating is one of the earliest clinical signs of a variety of autonomic neuropathies and neurodegenerative disorders, highlighting the diagnostic value of these techniques [7].

Our study found a significant rate (54.1%) of 85 patients with a moderate risk of developing CAN, and 45.9% with a low risk, while the percentage of high risk is zero, which is in line with a study carried out in 257 patients, in whom the SUDOSCAN allowed the detection of CAN and obtained the following 3 groups: 127 subjects without risk of developing CAN, 64 with a moderate risk and 66 with a high risk [17]. Another study conducted in China and enrolling 75 patients with type 2 diabetes (T2DM) and 45 non-diabetic (table 1) controls showed that patients with diabetic ANC (DCAN) and early DCAN had lower electrochemical skin conductance, which is positively correlated with severity, thus proving that SUDOSCAN is a reliable and feasible method for screening for DCAN in the Chinese diabetic population [18]. Casellini et al. demonstrated that SUDOSCAN is a sensitive tool for detecting neuropathy in diabetic patients, with a sensitivity of 78% and a specificity of 92%, equivalent or superior to clinical neuropathy scores [19]. And in India, Yajnik et al. have also conducted similar international studies [4].

**Table 1** Diagnostic efficiency of electrochemical skin conductance in the screening of diabetic cardiac autonomic neuropathy [18].

	Criterion*	Sensitivity (%)	Specificity (%)	+PV (%)	-PV (%)	TC (%)
Feet ESC	75.19 $\mu$ S	80.0	60.0	57.1	81.8	68.0
Hands ESC	75.76 $\mu$ S	76.7	75.6	67.6	82.9	76.0

ESC, electrochemical skin conductance; +PV, positive predictive value; -PV, negative predictive value; TC, total consistence rate. \*Criterion corresponding to the highest Youden index (feet ESC, 0.400; hands ESC, 0.522).

## 5. Conclusion

In conclusion, the risk score for cardiac autonomic neuropathy assessed by SUDOSCAN, and its ease of use and interpretation make it a good screening test for cardiac autonomic neuropathy. The assessment of the severity of microangiopathic complications in diabetic patients by the SUDOSCAN seems promising, as unrecognized complications are very frequent in this context.

## Compliance with ethical standards

### Acknowledgments

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### Disclosure of conflict of interest

No conflict of interest.

### Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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