

ANSIScope™: Can it be the Crystal Ball of Cardiac Anesthesia?

Abstract

Background: Autonomic dysfunction (AD) is infrequently evaluated preoperatively despite having profound perioperative implications. The ANSIScope™ is a monitoring device that quantifies AD. This study aims to determine the potential of the device to predict hypotension following anesthetic induction, occurrence of arrhythmias, and inotrope requirement for patients undergoing off-pump coronary artery bypass surgery (OPCAB). **Study Design:** Prospective observational double-blinded study. **Materials and Methodology:** Seventy-five patients undergoing OPCAB had their autonomic function assessed by ANSIScope™. They were classified into four groups based on their AD and compared to perioperative adverse events. **Results:** Patients with diabetes had a higher ANSindex ($P = 0.0263$). They had a greater decrease in systolic blood pressure ($P = 0.001$) and mean arterial pressure ($P = 0.004$) postinduction, had an increased incidence of arrhythmias ($P = 0.009$), required higher inotropic support immediately ($P = 0.010$) and at 24 h after surgery ($P = 0.018$), and longer duration of postoperative ventilation ($P < 0.001$). They also had a higher incidence of emergency conversion of OPCAB to on-pump surgery ($P = 0.009$). **Conclusions:** An increased association between AD as quantified by the ANSIScope™ and perioperative adverse outcomes was observed. An increased rate of emergency conversion of OPCAB to on-pump surgery with higher dysfunction was noted. The authors opine that the threshold for conversion must be lower in patients deemed to be at a higher risk. Proper evaluation of the autonomic nervous system empowers the anesthesiologist to anticipate and adequately prepare for complications.

Keywords: Autonomic dysfunction, ANSIScope™, arrhythmia, cardiac surgery, conversion, postoperative ventilation

Introduction

Autonomic nervous system (ANS), which includes the sympathetic and parasympathetic divisions, is a key regulator of the cardiovascular system. Both the divisions work in tandem to maintain homeostasis. Various clinical conditions such as diabetes, myocardial ischemia, and familial dysautonomia can lead to an imbalance in the system. This results in an increased incidence of perioperative complications such as postanesthetic hypotension, arrhythmias, coronary artery spasm, stroke, and sudden cardiac death. Despite this, the ANS is not routinely evaluated in the preoperative period.^[1,2]

Heart rate variability (HRV), reflecting sympathovagal balance, has been used as a prognostic factor in assessing cardiovascular autonomic neuropathy. Ewing's battery of clinical tests, which include heart rate response to Valsalva maneuver and deep breathing, blood

pressure variation with postural change, and sustained handgrip, have been in use since the 1970s to diagnose impaired HRV.^[3] However, these tests are time-consuming and require active patient participation, and instantaneous objective quantification of autonomic dysfunction (AD) is difficult.

ANSIScope™ (Dyansys Inc., California, USA) is a noninvasive device that overcomes the shortcomings of the clinical tests by quantifying AD. It gives a real-time graphical representation of the interaction between sympathetic and parasympathetic systems. It uses the principle of scale covariance obtained from the analysis of 572 successive R-R interval recordings of the electrocardiography (ECG). The absence of coupling between these two systems is extrapolated to quantify the percentage of AD (ANSindex). Higher percentage translates to greater sympathetic predominance.^[4,5]

The aim of the researchers was to determine the relationship between the AD, as quantified by the ANSIScope™,

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and postanesthesia hypotension, arrhythmias, and inotrope requirement following cardiac revascularization surgery.

Materials and Methodology

Study design

This study design was a prospective double-blinded observational clinical study.

Criteria

After obtaining Institutional Ethical Committee clearance, all patients scheduled to undergo elective off-pump coronary artery bypass grafting (OPCAB) at a tertiary cardiac care center were included in the study.

The exclusion criteria were patient refusal, combined valve and CABG procedures, elective on-pump CABG (ONCAB), and emergency and redo procedures; patients with preoperative arrhythmias and in cardiac failure; and patients on preoperative intra-aortic balloon pump and/or inotropic support.

Study protocol

Informed and written consent was obtained from all the patients who enrolled for the study. Demographic data, comorbid conditions, medications, and relevant preoperative investigation reports were noted. All patients received appropriate preanesthetic instructions, which included anxiolytic premedication and continuation of beta-blockers on the morning of the surgery, if any.

Autonomic dysfunction quantification

ANSiscope™ was used to determine the percentage of AD before anesthetic induction. ECG electrodes were attached to the palmar aspects of both the wrists and above the medial malleolus of both the lower limbs, with the patient lying supine and undisturbed, and the leads were connected to the device. Based on the ANSindex obtained after serial R-R interval analysis [Figure 1a and b], patients were classified into different groups as described below:^[4]

- Group 0 (Healthy) – <13.5%
- Group 1 (Early dysfunction) – 13.5%–23%

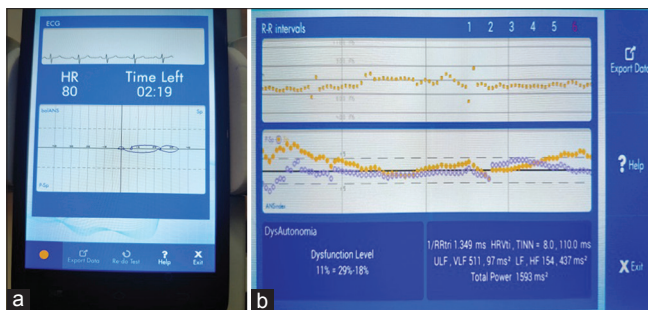


Figure 1: (a) ANSiscope™ monitor in the process of recording serial R-R intervals. (b) Graphical representation of sympathovagal interaction with ANSindex displayed at the end of analysis. (Orange - Sympathetic system, Blue - parasympathetic system)

- Group 2 (Late dysfunction) – 24%–50%
- Group 3 (Advanced dysfunction) – >51%.

Anesthetic induction

The anesthesiologist assigned to the patient had a minimum experience of 5 years in managing OPCAB cases. A large bore peripheral intravenous access and radial arterial line were secured under local anesthesia. The baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded. All patients received standardized titrated doses of induction agents – midazolam 0.05 mg/kg, fentanyl 5 µg/kg, vecuronium – 0.1 mg/kg, lidocaine – 1.5 mg/kg, and propofol titrated to effect. A second reading of SBP, DBP, and MAP was obtained 3 min postinduction and before intubation. Patients were intubated with appropriate sized endotracheal tube and anesthesia was maintained with 50:50 oxygen and air. Sevoflurane was the inhalational agent of choice. Revascularization was performed by professors of cardiac surgery with a minimum of 8 years of experience in the same.

Data collection

A person blinded to the ANSindex obtained performed data collection. In addition to the blood pressure readings, the occurrence and nature of arrhythmias up to 48 h, conversion to on-pump surgery, and inotrope score immediately, at 24 h and at 48 h postsurgery were noted. The duration of postoperative ventilation and the development of any other complications were recorded.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N. Y., USA). Categorical variables were analyzed using Chi-square test and continuous variables were analyzed with ANOVA test. Continuous variables were expressed as mean ± standard deviation. Student's *t*-test was used to compare mean values. $P < 0.05$ was considered statistically significant.

Results

Seventy-five patients (16 female and 59 male) satisfied the inclusion criteria and consented to participate in the study. Demographic data [Table 1a and Figure 2a] were comparable. Of the 75 patients, 49 (65%) had AD.

Of a total of 49 patients with dysfunction, 30 (61.22%) were diabetic. There was a significant association between diabetes and AD (71.42% of diabetics had AD as compared to 57.5% in nondiabetics, $P = 0.0263$).

Since beta-blockers can influence HRV, their effect on AD was considered. The degree of AD was found to be higher in patients not on beta-blockers (36% mean AD in those not on beta blockers vs. 27% in those on beta-blockers).

Comparing the preinduction SBP, DBP, and MAP, the difference in the percentage fall in blood pressure postinduction was analyzed between the groups. Patients with AD had a significantly greater percentage fall in SBP and MAP [Table 1b]. The greatest difference was seen in the group with late dysfunction when compared to normal patients.

The incidental finding during interpretation of intraoperative data was a higher rate of conversion of OPCAB to ONCAB with greater dysfunction ($P = 0.009$). The overall conversion rate was 25.3%, and 22.6% cases were emergency conversions. Eighty-nine percent of the patients, who had to be converted, had AD [Table 1c and Figure 2b]

The inotrope requirement at immediate, 24 h, and 48 h postsurgery was analyzed. Vasoactive inotropic score was

used (1* dopamine in $\mu\text{g}/\text{kg}$, 1* dobutamine $\mu\text{g}/\text{kg}$, 100* adrenaline in $\mu\text{g}/\text{kg}$, and 100* noradrenaline in $\mu\text{g}/\text{kg}$). Patients with and without AD were compared for inotrope requirement. Those with dysfunction had a significantly higher inotropic score immediate postsurgery ($P = 0.01$) and at 24 h postsurgery ($P = 0.023$). However, at 48 h, there was no difference in the score in between the groups [Table 2a and b].

The authors also noted the occurrence and nature of arrhythmias during the intra- and postoperative period. A total of 19 (25.3%) patients had arrhythmias. Nearly 95% of the patients who had arrhythmias had AD ($P = 0.009$, Table 3a). Ventricular arrhythmias were more frequent than atrial arrhythmias (68.42% vs. 31.57%).

Patients with greater degree of AD required significantly longer duration of postoperative ventilation ($P < 0.001$, Table 3b).

Discussion

Despite having a profound influence on the cardiovascular system, the ANS is rarely evaluated in preoperative patients.^[1] Literature review has shown that AD can result in sympathetic predominance, causing increased workload on the heart, endothelial dysfunction, arrhythmias, stroke, and sudden death.^[2] The frequency of these complications is highest in the early hours of the morning and on Monday in employed patients, which concurs with time of sympathetic predominance.^[2,6,7]

The major causative factors for AD in cardiac surgical patients are diabetes and myocardial ischemia.^[8-10] In the present study, thirty patients were found to have type 2 diabetes, of whom 71.42% were found to have AD. However, Ziegler *et al.*, in their study of 1171 patients, reported a much lower incidence of dysautonomia (22.1%) in type 2 diabetics.^[8] Diabetes has known to cause CAN by inducing oxidative and nitrosative stress in the fibers innervating the heart. Persistent hyperglycemia leads to accumulation of sorbitol and alters the NAD: NADH ratio, resulting in direct injury to the nerves.^[9]

Hypotension during anesthesia has been associated with worse postoperative patient outcome.^[10,11] One of the

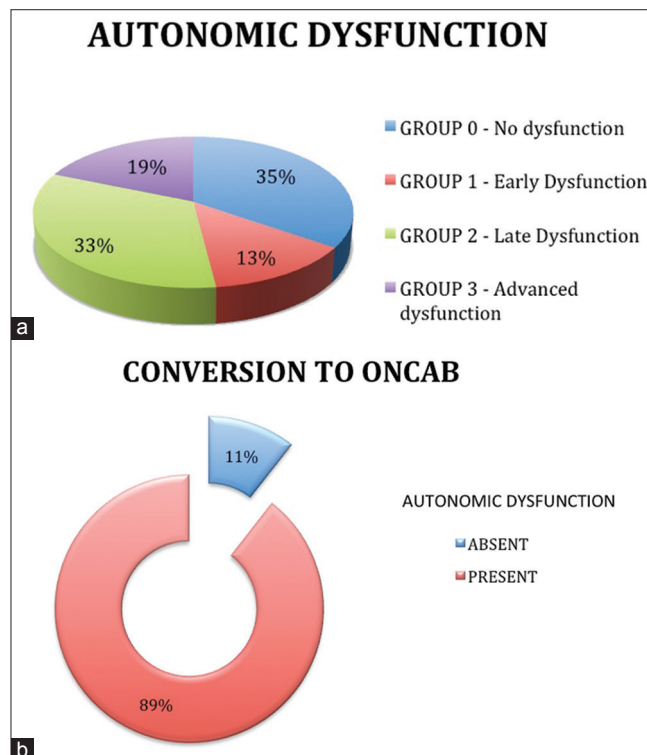


Figure 2: (a) Percentage-wise distribution of patients in each group. (b) Conversion to elective on-pump coronary artery bypass grafting in patients with autonomic dysfunction

Table 1a: Demographic characteristics

	AD classification (mean±SD)				P
	Group 0, (n=26)	Group 1, (n=10)	Group 2, (n=25)	Group 3, (n=14)	
Age (years)	59.38±7.574	58.50±9.192	60.04±7.197	56.36±7.292	0.526
Height (cm)	160.50±7.855	161.3±9.154	160.92±10.866	159.79±7.485	0.976
Weight (kg)	63.69±8.930	60.90±7.534	67.32±10.832	65.86±7.502	0.251
BMI	24.7±3.14	23.35±1.408	26.05±3.874	25.79±2.519	0.104
Sex					
Female	2	3	6	5	0.182
Male	24	7	19	9	

SD: Standard deviation, BMI: Body mass index, AD: Autonomic dysfunction

objectives of the researchers was to assess the ability of the ANSscope to predict hypotension after induction of general anesthesia. Patients with late dysfunction (Group 2) had a greater percentage fall in SBP, DBP, and MAP when compared to normal patients (Group 0). The fall in SBP ($P = 0.001$) and MAP ($P = 0.004$) was statistically significant. This finding concurs with Latson *et al.*^[12] and Hanss *et al.*,^[13] who demonstrated a greater incidence of hypotension after general anesthesia administration in patients with AD, using clinical tests and HRV to detect AD. ANSindex was used as a tool to predict postspinal hypotension in parturients undergoing elective lower segment cesarean section by Prashanth *et al.*^[14] in their study comprising 108 patients. The area under receptor operator characteristic curve for ANSindex as a solitary predictor for hypotension was 0.737. The use of anesthetic drugs decreases the capacity to release residual catecholamines in patients with dysautonomia.^[14]

A total of 19 patients developed perioperative arrhythmias, of whom 18 (94.7%) had AD ($P = 0.009$). Although arrhythmias of atrial origin are most common after cardiac surgery,^[15] we found a higher incidence of ventricular arrhythmias (31.57% vs. 68.42%). Chen *et al.* have documented an increased association between arrhythmias and sudden cardiac death due to abnormal patterns of sympathetic reinnervation.^[6]

The Autonomic Tone and Reflexes After Myocardial Infarction investigators opine that recognizing the inadequacy of vagal tone empowers the treating physician to target the loss of antifibrillatory effects.^[7] The present

study also demonstrates a greater degree of AD in patients not on beta-blockers (mean AD of 36%) when compared to those on beta blockers (mean AD of 27%) although it was not statistically significant ($P = 0.086$).

A serendipitous outcome encountered by the researchers was a significant increased rate of conversion of OPCAB to ONCAB in patients with AD ($P = 0.009$). The most common indication was severe hypotension during obtuse marginal grafting. Edgerton *et al.*^[16] in their study found that the patients who underwent an urgent-emergent conversion (in comparison with elective conversion) had a higher rate of postoperative cardiac arrest, MI, and multisystem organ failure. Lim *et al.*^[17] have described the 5-year survival rate to be 83.5% in the off-pump group and 73.9% in the conversion group. The CORONARY trial (Coronary artery bypass grafting Off or On Pump Revascularization Study), which studied 4718 patients undergoing CABG, also found a higher incidence of stroke, MI, renal failure, and death in emergent conversions, whereas the elective conversions were comparable with off-pump surgeries.^[18] In the current study, 89% of the patients who had to be converted were found to have AD. The overall conversion rate was 25.3%, with 22.6% of them being emergency conversions. Various studies have investigated the risk factors favoring conversion, ranging from advanced age, absence of beta blocker therapy, low ejection fraction, prior MI, cardiac failure, etc. However, there is limited literature implicating AD as a potential risk factor for conversion.

The ANSindex was used to compare the requirement of inotropes immediately, at 24, and 48 h after surgery. There was a significant higher inotrope score at immediate ($P = 0.010$) and at 24 h postsurgery ($P = 0.018$) in patients with AD, whereas there was no difference between the groups at 48 h.

Prolonged postoperative ventilation contributes to significant morbidity.^[18] Of the 75 patients studied, 2 patients had a requirement for ventilation for >48 h. Both had advanced AD (Group 3). Five patients required ventilation ranging from 20 to 48 h. All of them had either late or advanced dysfunction (Group 2/3). There was a significant prolongation of duration of ventilation in patients with AD ($P < 0.001$). Positive pressure ventilation decreases the venous return and cardiac output.^[19] Patients with AD who already have a maximally activated

Table 1b: Comparison between the mean percentage changes from baseline in systolic blood pressure, diastolic blood pressure, mean arterial pressure between the groups

	AD classification				P
	Group 0, (n=26)	Group 1, (n=10)	Group 2, (n=25)	Group 3, (n=14)	
Mean SBP percentage decrease	26.33	29.18	37.29	30.17	0.001
Mean DBP percentage decrease	23.12	24.16	30.21	22.82	0.07
Mean MAP percentage decrease	24.91	26.71	33.71	26.30	0.004

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, MAP: Mean arterial pressure, AD: Autonomic dysfunction

Table 1c: Conversion to on-pump CABG compared between the groups

	AD classification				Total	χ^2	P
	Group 0 (n= 26)	Group 1 (n=10)	Group 2 (n= 25)	Group 3 (n=14)			
Conversion to ONCAB							
No	24 (42.9)	9 (16.1)	16 (28.6)	7 (12.5)	56 (74.6)	11.528	0.009
Yes	2 (10.5)	1 (5.3)	9 (47.4)	7 (36.8)	19 (25.3)		
Total	26 (34.6)	10 (13.3)	25 (33.3)	14 (18.6)	75 (100)		

ONCAB: On-pump CABG, AD: Autonomic dysfunction

sympathetic system may be incapable of increasing their reserves to counteract the effects of positive pressure ventilation.^[20] This can account for the increased inotrope requirement and increased duration of ventilation.

Increasing age has been associated with declining autonomic functions.^[21]

The current therapy for AD aims at early diagnosis, regular screening and follow-up, exercise regimens, adequate glycemic control, and management of cardiovascular risk factors. Medical therapy available includes beta blockers,

aldose reductase inhibitors (epalrestat and fidarestat), ACE inhibitors, prostaglandin analogs, and alpha-lipoic acid, apart from specific medication for symptoms such as erectile dysfunction and loss of bladder control.^[22]

Limitations

The quantification of dysfunction as provided by the ANSiscope™ was not compared with any other method to assess AD. The device cannot be used in the presence of arrhythmias.

Conclusions

AD is commonly encountered in the perioperative cardiac setting and contributes to significant morbidity. Despite having a profound influence on the cardiovascular system, the ANS is rarely evaluated on a routine basis preoperatively. ANSiscope™ is a time efficient, easy to use, noninvasive device to quantify AD. The researchers noticed an increased association between dysfunction and diabetes, occurrence of arrhythmias, postoperative duration of ventilation, and inotrope requirement. One of the significant findings was the increased rate of emergency conversion of OPCAB to ONCAB with higher degree of dysfunction, which is again proven to be associated with higher morbidity and mortality. The authors opine that the threshold for conversion must be lower in patients deemed to be at risk. Adequate evaluation of the ANS empowers the anesthesiologist to anticipate and formulate tailor-made plans for patients as required.

Acknowledgments

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Table 2a: Inotrope score-immediate postsurgery

	AD		Total	χ^2	P
	No, n (%)	Yes, n (%)			
Inotrope score (immediate)					
A	8 (66.7)	4 (33.3)	12	11.402	0.010
B	15 (41.7)	21 (58.3)	36		
C	3 (23.1)	10 (76.9)	13		
D	1 (7.1)	13 (92.9)	14		
Total	27 (36)	48 (64)	75		

A: No inotrope, B: 1-5 score, C: 6-10 score, D: >11 score.
AD: Autonomic dysfunction

Table 2b: Inotrope score-24 h postsurgery

	AD		Total	χ^2	P
	No, n (%)	Yes, n (%)			
Inotrope score (24 h)					
A	20 (54.05)	17 (45.9)	37	11.892	0.018
B	5 (26.3)	14 (73.68)	19		
C	2 (16.66)	10 (83.33)	12		
D	0	5 (100)	5		
Total	27 (36)	48 (64)	75		

A: No inotrope, B: 1-5 score, C: 6-10 score, D: >11 score.
AD: Autonomic dysfunction

Table 3a: Incidence of arrhythmias and autonomic dysfunction

	AD classification				Total	χ^2	P
	Group 0, n (%)	Group 1, n (%)	Group 2, n (%)	Group 3, n (%)			
Arrhythmia							
No	25 (44.6)	8 (14.3)	15 (26.8)	8 (14.3)	56 (74.6)	11.612	0.009
Yes	1 (5.3)	2 (10.5)	10 (52.6)	6 (31.6)	19 (25.3)		
Total	26 (34.6)	10 (13.3)	25 (33.3)	14 (18.6)	75 (100)		

AD: Autonomic dysfunction

Table 3b: Ventilator hours and autonomic dysfunction

	AD classification				Total	χ^2	P
	Group 0, n (%)	Group 1, n (%)	Group 2, n (%)	Group 3, n (%)			
Ventilator hours							
A	17 (58.6)	7 (24.1)	2 (6.9)	3 (10.3)	29 (39.7)	35.696	0.000
B	9 (20.9)	1 (2.3)	21 (50.0)	11 (25.6)	42 (57.5)		
C	0	1 (50.0)	1 (50.0)	0	2 (2.7)		
Total	26 (35.1)	9 (12.2)	24 (32.8)	14 (18.9)	73 (100)		

A: <6 h, B: 7-24 h, C: >24 h. AD: Autonomic dysfunction

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Conflicts of interest

There are no conflicts of interest.

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