

## Changes of Hemodynamics and Blood Glucose during Tracheal Intubation in the Geriatrics with Different Glycosylated Hemoglobin Levels

Xiaoguang Guo<sup>1</sup>, Xiaoyan Zhou<sup>2</sup>, Jie Sun<sup>3</sup>, Yanning Qian<sup>3\*</sup>

<sup>1</sup>Department of Anesthesiology, First Affiliated Hospital, Zhengzhou University, Zhengzhou, China

<sup>2</sup>Department of Anesthesiology, Nanjing eight one Hospital of People's Liberation Army, Nanjing, China

<sup>3</sup>Department of Anesthesiology, First Affiliated Hospital, Nanjing Medical University, Nanjing, China

\*Corresponding author: Yanning Qian, Department of Anesthesiology, The First Affiliated Hospital of Nanjing Medical University, No. 300, Guangzhou Road, Nanjing 210029, China, Tel: +86 25 8371 8836; Fax: +86 25 8420 0723; E-mail: [yanning\\_qian@163.com](mailto:yanning_qian@163.com)

### Abstract

**Background:** The severe cardiovascular response following tracheal intubation has threatened geriatrics' safety. HbA1c may be an independent risk predictor for the outcome of cardiovascular disease and/or DM. We investigated the relationship between preoperative HbA1c levels and changes of hemodynamic and blood glucose (Glu) during tracheal intubation in geriatrics.

**Methods:** 112 geriatric non-cardiac surgery patients undergoing general anesthesia were divided into 4 groups according to HbA1c levels (Group A, B, C and D). Mean arterial pressure (MAP) and heart rate (HR) were recorded before anesthesia induction ( $T_0$ , just before intubation ( $T_1$ ), at intubation ( $T_2$ ), 1, 2, 3, 5, 8 and 10 minutes after intubation ( $T_{3-8}$ ). Glu Levels were measured at  $T_0$ ,  $T_1$ ,  $T_6$  and  $T_8$ .

**Results:** Compared with group A or B, MAP decreased markedly at  $T_{1-8}$  in group C or D ( $P < 0.05$ ). Compared with  $T_0$ , HR decreased markedly at  $T_1$ ,  $T_{6-8}$  in group C and at  $T_{1-3}$ ,  $T_{5-8}$  in group D ( $P < 0.05$ ). The  $\Delta$  (the difference value of MAP between  $T_0$  and  $T_8$  points) and the  $\Delta$  (the difference value of HR between  $T_0$  and  $T_8$  points) of all patients were highly correlated with preoperative HbA1c levels [ $\Delta$  (mmHg) =  $-9.436 \text{ HbA1c} + 25.94$ ,  $R^2 = 0.368$ ;  $\Delta$  (bpm) =  $-6.172 \text{ HbA1c} + 26.842$ ,  $R^2 = 0.208$ ].

**Conclusion:** Preoperative high HbA1c level may contribute to significant hemodynamic changes and significant increased blood Glucose levels after tracheal intubation, especially for elder patients with HbA1c  $> 7\%$ .

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**Keywords:** Geriatrics; Glycosylated hemoglobin; Tracheal intubation; Hemodynamic; Blood glucose



### Introduction

Plasma haemoglobin A1c (HbA1c) represents the most prevalent glycohemoglobin (GHb) which is formed by the slow irreversible, non-enzymatic glycation of valine and lysine residues in the haemoglobin molecule<sup>[1]</sup>. As the postsynthetic modifications of HbA irreversibly form GHb, the HbA1c concentration constitutes a reliable, integrated measure of the average blood glucose concentration over the life spans of circulating red cells. Measurement of HbA1c is widely used in clinical practice to reflect mean ambient fasting and postprandial gly-

caemia over a 2 – 3 months period<sup>[2,3]</sup>. HbA1c level has added to a diagnosis criteria of diabetes mellitus (DM) by the American Diabetes Association (ADA) in 2010<sup>[4]</sup>. As the increasing incidence of cardio-cerebrovascular complications in DM patients, the relationship between the HbA1c level and the cardio-cerebrovascular complications has sparked growing interests within the past years. U. Krishnamurti et al reported HbA1c was an independent risk predictor for the outcome of cardiovascular disease and/or DM<sup>[5]</sup>.



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Anesthesia induction is the essential process of anesthesia. We should keep equability during the induction, avoid oxygen deficit and the cardiovascular suppression, ensure adequate anesthesia depth, and eliminate the stress reaction of tracheal intubation. It has been demonstrated that elderly patients have an increased risk of hypotension during anesthesia induction<sup>[6,7]</sup>. As we know, the aged people usually represent with degenerative organs function, especially the cardiovascular system. DM accelerated the degenerative changes of cardiovascular system, thus lead to instability of hemodynamics, unbalance of oxygen supply, cardiovascular intolerance to anesthesia induction, increased perioperative complication, and mortality<sup>[8,9]</sup>. A preliminary study showed<sup>[10]</sup> the elevated HbA1c levels of elderly DM before surgery was a predictor for tracheal intubation response variation. The response would be more obvious while the level of HbA1c exceeded 6.5%. But no research focuses on the relationship between different HbA1c levels and intubation response.

In the present study, we observed the changes of hemodynamics and blood glucose levels during tracheal intubation in elderly patients with different preoperative HbA1c levels, especially HbA1c > 7%, in order to explore whether the HbA1c level was an preoperative predictor of the cardiovascular response to tracheal intubation in aged DM patients.

## Methods

### Subjects

Patients aged 65 - 74 years with American Society of Anesthesiologists status I II and scheduled for elective non-cardiac surgery under general anesthesia in our hospital from December of 2010 to May of 2011 were recruited for the study after approval by the Ethics Committee of Jiangsu Province Hospita and patients' written informed consent. We excluded patients with baseline artery blood pressure > 160/95 mmHg, intubation for more than once and a history of taking medications that might affect the cardiovascular system or block adrenergic responses to intubation. In no case were vasoactive medications used during induction. Based on their preoperative HbA1c levels, all patients were divided into 4 groups: the Group A (HbA1c < 5.7%, 24 cases), the Group B (5.7% ≤ HbA1c ≤ 6.4%, 34 cases), the Group C (6.5% ≤ HbA1c < 7%, 27 cases), the Group D (7% ≤ HbA1c ≤ 8%, 27 cases).

### Anesthesia and monitoring

All the patients received intravenous access followed by lactate Ringer's solution at 8 ml/Kg/h and radial artery pressure monitoring on the arrival to the operating room. The blood samples were collected for the levels of HbA1c by Latex Agglutinate Reaction Kit (Shanghai Shen Suoyou Medical Diagnostic Products Ltd.). The detection of glucose levels of all patients was performed by collecting blood samples from the patients' right index fingers, and then examining using Johnson Blood Glucose Meter.

All patients underwent venous injection of midazolam 0.05 mg/kg, propofol 1.5 mg/kg, fentanyl 3 μg/kg and atracurium Besilate 0.15 mg/kg at a constant speed within 60 seconds and then received orotracheal intubation 2.5 minutes later by the same anesthetist. Every patient received intermittent positive pressure ventilation with tidal volume 6 ~ 8 ml/Kg, rate 12 ~ 13

bpm and ET CO<sub>2</sub> was kept at 35 ~ 40 mmHg. In the study no anesthetics was given through the vein or respiratory tract except the drugs administered for induction and any implementation of the operations on the patients were forbidden including physical movement, catheterization and preparation for the operation area.

MAP and HR were recorded before anesthesia induction (T<sub>0</sub>), just before intubation (T<sub>1</sub>), at intubation moment (T<sub>2</sub>), 1, 2, 3, 5, 8, and 10 min after intubation (T<sub>3-8</sub>). The level of the artery blood glucose were respectively recorded at T<sub>0</sub>, T<sub>1</sub>, T<sub>6</sub> and T<sub>8</sub> using the fast blood glucose meter (Bayer Health Care, Germany).

### Statistical Analyses

All the data were presented as means ± SD. Statistical analysis was performed by the SPSS 13.0 for Windows statistical software (SPSS Inc, Chicago, IL, USA). The data within the groups were compared with one way analysis of variance and the comparison between the two groups used covariance analysis. P-value less than 0.05 were considered as statistical significant. The major variables were also analyzed with linear correlation (R = correlation). 0.5 < R ≤ 0.8 was considered as significant correlation and 0.8 < R ≤ 1 means a strong correlation.

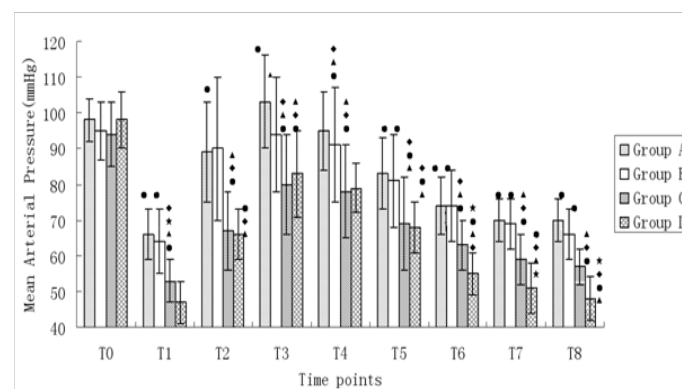
## Results

**Patients Charateristics:** There were no significant differences in the gender, age, weight and intubation time among the four groups (Table 1)

**Table 1:** Patients Charateristics.

Group	Cases	Sex (male/female)	Weight (Kg)	Age(year)	Intubation time (s)
A	24	12/12	60.21 ± 8.17	68.25 ± 4.95	54 ± 3
B	34	25/9	61.56 ± 9.67	66.18 ± 4.81	55 ± 5
C	27	16/11	63.93 ± 10.64	68.26 ± 4.78	54 ± 4
D	27	18/9	63.04 ± 9.59	67.11 ± 3.83	55 ± 3

### Changes of MAP during anesthesia induction (Figure 1)

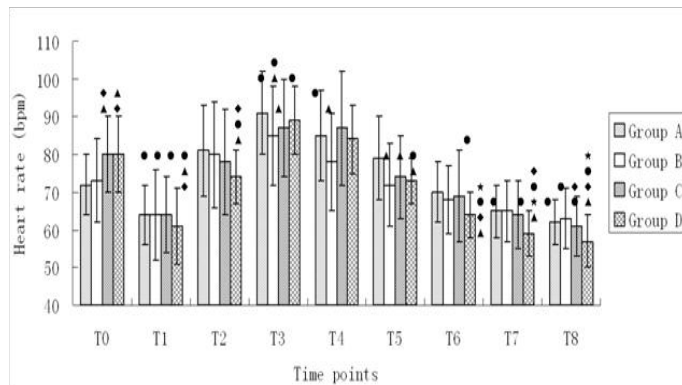


**Figure 1:** Changes of MAP during anesthesia induction. Compared with T<sub>0</sub>, ●P < 0.05; Compared with A, ▲P < 0.05; Compared with B, ♦P < 0.05; Compared with C, \*P < 0.05.

MAP at T<sub>0</sub> in all groups had no significant difference (P > 0.05). MAP was significantly decreased at T<sub>1</sub> in all the groups

( $P < 0.05$ ). In group A, MAP at  $T_3$  was higher than that of  $T_0$  ( $P < 0.05$ ), but in other groups MAP had a decrement tendency. MAP at  $T_{5-8}$  in group A and B and MAP at  $T_{2-8}$  in group C and D were significantly lower than their baseline value ( $P < 0.05$ ). Compared with group A and B, MAP at all time points ( $T_{1-8}$ ) in group C and D was obviously lower ( $P < 0.05$ ). Compared with group C, MAP at  $T_1$  and  $T_{6-8}$  in group D decreased significantly ( $P < 0.05$ ).

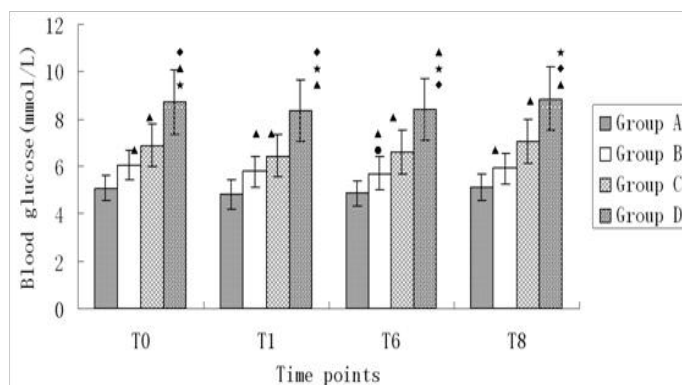
**Changes of HR during anesthesia induction (Figure 2)**



**Figure 2:** Changes of HR during anesthesia induction. Compared with  $T_0$ , ● $P < 0.05$ ; Compared with A, ▲ $P < 0.05$ ; Compared with B, ◆ $P < 0.05$ ; Compared with C, \* $P < 0.05$ .

HR values of patients at  $T_0$  in group A and B had no significant difference ( $P > 0.05$ ). HR at  $T_0$  in group C and D was higher than that in group A and B ( $P < 0.05$ ). Compared with HR at  $T_0$  in all four groups, HR obviously decreased at  $T_1$  ( $P < 0.05$ ). HR was high at  $T_{3,4}$  in group A and at  $T_3$  group B and D ( $P < 0.05$ ). HR significantly decreased at  $T_{7-8}$  in group A, at  $T_8$  in group B, at  $T_{6-8}$  in group C and  $T_{5-8}$ ,  $T_2$  at in group D ( $P < 0.05$ ). Compared with HR at different time points after induction in group A, HR dropped more significantly at  $T_{3-5}$  in group B, at  $T_3$ ,  $T_5$  in group C and at  $T_{1-2}$ ,  $T_{5-8}$  in group D ( $P < 0.05$ ). Compared with HR at different time points after induction in group B, HR significantly decreased at  $T_1$ ,  $T_8$  in group C and at  $T_{1-2}$ ,  $T_{6-8}$  in group D ( $P < 0.05$ ). HR was obviously lower at  $T_{6-8}$  in group D compared with that at the time points after induction in group C ( $P < 0.05$ ).

**Changes of blood glucose during anesthesia induction (Figure 3)**

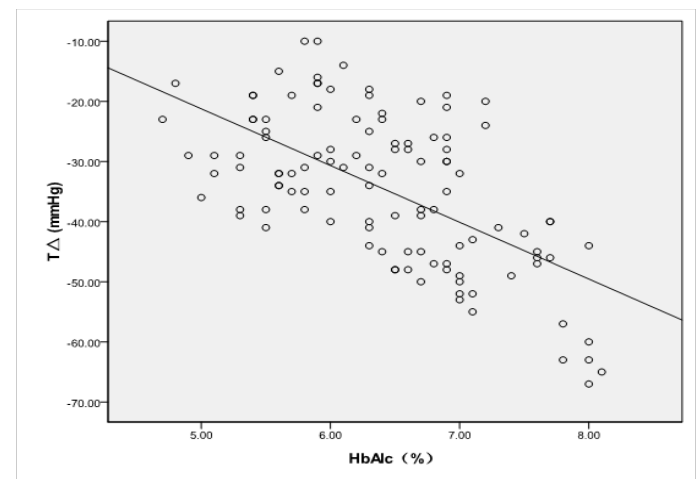


**Figure 3:** Changes of blood glucose during anesthesia induction. Compared with  $T_0$ , ● $P < 0.05$ ; Compared with A, ▲ $P < 0.05$ ; Compared with B, ◆ $P < 0.05$ ; Compared with C, \* $P < 0.05$

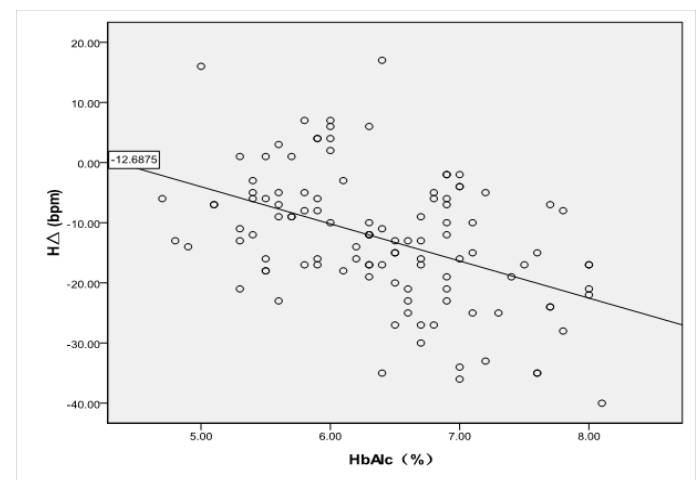
Glucose levels at all time points in four groups increased as the HbA1c levels, and this increased tendency had significant difference ( $P < 0.05$ ). There was no significant difference of glucose level at  $T_6$  in group B ( $P < 0.05$ ). There was no significant difference of glucose level in other groups ( $P < 0.05$ ).

**The correlation between preoperative HbA1c levels and changes of MAP (Figure 4), HR (Figure 5) and glucose level at all time points.**

The difference ( $T\Delta$ ) between MAP at  $T_0$  and that at  $T_0$  in all the patients was highly positively correlated to their preoperative HbA1c levels [ $T\Delta$  (mmHg) =  $-9.436 \text{ HbA1c} + 25.94$ ,  $R^2 = 0.368$ ,  $P < 0.001$ ]. The difference between HR at  $T_0$  and that at  $T_0$  in all the patients was positively correlated to their preoperative HbA1c levels [ $H\Delta$  (bpm) =  $-6.172 \text{ HbA1c} + 26.842$ ,  $R^2 = 0.208$ ,  $P < 0.001$ ]. The highly positive correlation also existed among preoperative HbA1c levels and glucose levels at  $T_0$ ,  $T_1$ ,  $T_6$  and  $T_8$  ( $T_{0\text{glu}} = 1.682 \text{ HbA1c} - 4.079$ ,  $R^2 = 0.739$ ,  $P < 0.001$ ;  $T_{1\text{glu}} = -4.079 + 1.682 \text{ HbA1c}$ ,  $R^2 = 0.715$ ,  $P < 0.001$ ;  $T_{6\text{glu}} = -4.124 + 1.642 \text{ HbA1c}$ ,  $R^2 = 0.718$ ,  $P < 0.001$ ;  $T_{8\text{glu}} = -4.419 + 1.741 \text{ HbA1c}$ ,  $R^2 = 0.737$ ,  $P < 0.001$ , respectively).



**Figure 4:**  $T\Delta$  = the difference value of MAP between  $T_0$  and  $T_8$ ;  $T\Delta$  had A statistically significant inverse correlation with the HbA1c levels [ $T\Delta$  (mmHg) =  $-9.436 \text{ HbA1c} + 25.94$ ,  $R^2 = 0.368$ ,  $P < 0.001$ ].



**Figure 5:**  $H\Delta$  = the difference valve of HR between  $T_0$  and  $T_8$ ; The  $H\Delta$  was statistically correlated with preoperative HbA1c levels [ $H\Delta$  (bpm) =  $-6.172 \text{ HbA1c} + 26.842$ ,  $R^2 = 0.208$ ,  $P < 0.001$ ].

## Discussion

HbA1c (Hemoglobin A1c, HbA1c), a form of hemoglobin, is measured primarily to identify the average blood Glu level over prolonged periods of time and suggested to be a golden standard for evaluating Glu level of DM for a long time. The Diabetic Guideline 2010 from the American Diabetes Association (ADA) added HbA1c  $\geq 6.5\%$  as a new dynamic criteria, and people with  $5.7\% \leq \text{HbA1c} \leq 6.4\%$  were considered as at a high risk of diabetes in the 2010 Diagnosis and classification of diabetes mellitus. Diabetes Care.

As a systemic disease, the diabetes can lead to the pathological changes of tissues and organs all over the body, especially the micrangiums, and the degree of the pathological changes depending on the course of disease and the Glu level<sup>[11]</sup>. Moreover, the cardio-cerebrovascular complications of the diabetics have been the major course of the death of DM<sup>[12,13]</sup>. Gustavson et al<sup>[14]</sup>, reported that the inflammatory markers such as C-reactive protein, fibrinogen, red blood cells subsidence ratio and white blood cells count in patients with coronary heart disease will increase with an increase of HbA1c levels, which suggested the increasing HbA1c levels may enhance the progression of coronary heart disease. In the Norfolk cohort of European prospective investigation of cancer and nutrition<sup>[15]</sup>, the value of HbA1c levels was examined as a predictor of death from cardiovascular in all causes in men, and the result showed that an increase of 1% HbA1c was associated with a 28% increase in risk of death. This effect remained in people without diabetes. These studies suggested that the HbA1c level before operation might be considered as an important predictor for the risk of cardiovascular events in diabetic patients.

In our study, MAP at all time points ( $T_{1-8}$ ) of group C and D was obviously lower than that of group A and B. MAP at all time points in group D was clearly below that in group C. This result showed that the higher the preoperative HbA1c levels was, the lower MAP would happen after anesthesia induction. As a result, high HbA1c levels led to long-term hyperglycaemia, which may enhance the glycosylation and protein of the protein on the inner surface of blood vessels, and the following increased advanced glycation end products promoted the progression of atherosclerosis. The high endothelin and reduced secretion of NO and prostacylin (PGI<sub>2</sub>) owing to high blood glucose may also contribute to the injury of vascular endothelial cell. The high blood glucose may directly injure the endothelial cell<sup>[16,17]</sup>. So the higher the blood glucose is, the more severe the vasomotorial dysfunction will be, which may lead to the large fluctuations of MAP.

According to the diabetes diagnostics guideline of ADA, patients in the group C and D were diagnosed with diabetes. The baseline HR of patients in group C and D was higher than that in group A and B. This result may be due to the impaired function of cardiac autonomic nervous system of diabetes patients. HR dropped more significantly at  $T_{3-5}$  in group B, at  $T_{3, T_5}$  in group C and at  $T_{1-2, T_{5-8}}$  in group D than that in group B ( $P < 0.05$ ). Compared with HR at different time points after induction in group B, HR decreased more sharply at  $T_1, T_8$  in group C and at  $T_{1-2, T_{6-8}}$  in group D ( $P < 0.05$ ). HR was obviously lower at  $T_{6-8}$  in group D compared with that at the time points after induction in group C ( $P < 0.05$ ). Such results reflected that the higher the HbA1c levels is, the weaker the acceleration of cardi-

ac autonomic nervous conduction is. One study reported that a significant hemodynamic change emerged after the endotracheal intubation of diabetes patients, including low HR, hypotension and decreased cardiac output<sup>[18]</sup>. Another studies showed that the diabetes complication and cardiovascular risk may be associated with the impairment of parasympathetic nerve function<sup>[19,20]</sup>. In group A, MAP at  $T_3$  was higher than that at  $T_0$ , and HR at  $T_3, T_4$  was also higher than that at  $T_0$ . This hemodynamic change was a normal stress response to tracheal intubation in older patients, which reflected the normal functions of cardiac autonomic nervous system in these patients.

HbA1c values may serve as biomarkers for glucose control during the perioperative period in patients with diabetes<sup>[21]</sup>. In the current study, patients with higher HbA1c had higher preoperative and operative blood glucose, which was consistent with the Moitra's results.

All the results of the present study indicated that the elder diabetics with higher HbA1c levels presented with significant hemodynamic changes especially when HbA1c  $\geq 7\%$ . The standards of medical care in diabetes 2010 of ADA recommended the HbA1c level in patients with diabetes should be regulated around 7% or below so as to reduce the incidence of microvascular and neurological complications. A previous prospective study of elevated HbA1c and increased risk of adverse outcome following surgical intervention by O'Sullivan CJ et al demonstrated that patients with or without diabetes with suboptimal HbA1c levels had a higher incidence of 30-day postoperative morbidity compared to those with optimal HbA1c levels and the high HbA1c level may have prognostic significance in patients without diabetes undergoing vascular surgery<sup>[22]</sup>. This previous result was consistent with that of our current study. Then the preoperative HbA1c level of the geriatrics should be paid great importance by the anaesthetists to make preoperative evaluation so as to maintain perioperative hemodynamics steadily and the balance of vital organs oxygen delivery and consumption.

The changes of MAP, HR at different time points in group A and B were less than those in group C and D. The blood glucose levels before and during the surgery in group B were higher than those in group A. Patients in group B (HbA1c 5.7% - 6.4%) classified as people at a high risk of diabetes in the ADA 2010, had over 10 times of the incidence of diabetes than patients with lower HbA1c levels and active interventions were needed. Long-term hyperglycaemia could facilitate the generation of HbA1c, and one study<sup>[23]</sup> showed that HbA1c decreased the erythrocyte deformability and increased the binding affinity with oxygen of red blood cells. A prospective cohort study demonstrated that HbA1c levels predict insulin sensitivity during surgery which was associated with an increased risk of major complications including mortality, heart failure, stroke, independent of the diabetic state<sup>[24]</sup>.

In our study, the changes of MAP and HR during induction and tracheal intubation in geriatrics had a significant correlation with the preoperative HbA1c levels. The intra-operative blood glucose levels at the four time points were respectively highly relevant to preoperative HbA1c levels. We acknowledge several limitations of our study. Colayco et al reported that high-risk patients with type 2 diabetes who failed to decrease HbA1c to  $< 8\%$  were at increased risk for cardiovascular events<sup>[25]</sup>. We didn't collect enough cases of elder patients with HbA1c  $> 8\%$  within limited duration, which may be the reason for the defi-

ciency of more remarkable hemodynamic changes.

In conclusion, our current study demonstrated the geriatrics with higher HbA1c level presented with significant hemodynamic changes and significant increased blood glucose levels after tracheal intubation, especially for elder patients with HbA1c > 7%, and these changes were highly correlated with the preoperative HbA1c levels. Thus, it suggested that elevated glycosylated hemoglobin level could predict severe changes of hemodynamics and blood glucose level during tracheal intubation in elderly diabetics.

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