European Review for Medical and Pharmacological Sciences 2021; 25: 293-300

The correlation between tissue Doppler imaging and N-terminal pro-brain natriuretic peptide concentration during left ventricular diastolic function recovery after coronary artery bypass grafting

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Abstract. – OBJECTIVE: This study aims to evaluate the changes in left ventricular diastolic function after coronary artery bypass grafting through tissue Doppler imaging (TDI) and N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration and the correlation between the two.

PATIENTS AND METHODS: A total of 133 patients who underwent coronary artery bypass grafting between January 2016 and December 2018 were included in this study. Echocardiography and NT-proBNP concentration were reviewed pre-operation, 1 month post-operation, and 3-6 months post-operation. The transmitral peak flow velocity (E) of the mitral valve was measured at each of the three-time points using spectral Doppler imaging. The mitral annulus displacement (Ea peak and Aa peak) was then measured at each of the time points using TDI, and the E/Ea ratio was calculated. Subsequently, the correlation of the E value, Ea value, and E/Ea ratio with NT-proBNP concentration was statistically analyzed.

RESULTS: The data obtained at the three-time points were compared with the respective concentrations of NT-proBNP. Multiple linear regression analysis revealed a correlation between NT-proBNP concentration and E value, Ea value, and E/Ea ratio.

CONCLUSIONS: Left ventricular diastolic function gradually recovered at 1 month and 3–6 months after coronary artery bypass grafting. There was a correlation between TDI-related values and NT-proBNP concentration.

Key Words:
Tissue Doppler imaging, NT-proBNP, Coronary artery bypass grafting, Left ventricular diastolic function, Relevance.

Abbreviations

CAHD: Coronary atherosclerotic heart disease; CABG: Coronary artery bypass grafting; TDI: tissue Doppler imaging; NT-proBNP: N-terminal pro-brain natriuretic peptide; A4C: Apical four-chamber; E: Transmitral peak flow velocity; Ea: Peak early diastolic velocity of the mitral annulus; PCWP: Pulmonary capillary wedge pressure.

Introduction

Coronary atherosclerotic heart disease (CAHD) is a life-threatening disease, and its incidence is increasing every year[1,2]. In addition to the extensively used coronary stent implantation for the treatment of CAHD, coronary artery bypass grafting (CABG) has also become widely accepted. For patients with lesions in multiple coronary artery branches, CABG remains a common method of treatment[3-6].

Previous studies have focused on left ventricular systolic function changes after coronary artery ischemia-reperfusion but have paid less attention to left ventricular diastolic function (LVDF). However, myocardial ischemia not only affects systolic function but also leads to diastolic dysfunction, and the prognosis of patients with diastolic heart failure is as poor as that of patients with systolic dysfunction-induced heart failure. Studies have also shown that, although the systolic function of acute myocardial ischemia returns to normal within 24 hours after the successful percutaneous coronary intervention (PCI), diastolic dysfunction still remains.

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Tissue Doppler imaging (TDI) is a technical indicator used to evaluate myocardial function recovery after CABG. Detection of the N-terminal brain natriuretic peptide precursor (NT-proBNP) is also of great value in the diagnosis and evaluation of symptomatic heart failure, although there is little information on the significance of NT-proBNP in the evaluation of asymptomatic diastolic dysfunction. The aim of the present study is to investigate the recovery of LVDF 1 month and 3-6 months after CABG using TDI data and NT-proBNP concentration and to identify a correlation between TDI parameters and NT-proBNP levels in the recovery of LVDF after CABG[7-12].

Patients and Methods

Patient Selection

A total of 133 patients who underwent off-pump CABG in the First People's Hospital of Lanzhou and Gansu Cardiovascular Institute between January 2016 and December 2018 were included in this study. The sample consisted of 103 male patients and 30 female patients, aged 42-85, with an average age of 58.7 ± 8.4 years.

Using the New York Heart Association (NYHA) classification, 31 of the cases were classified as Grade II, 77 as Grade III, and 25 as Grade IV. Coronary angiography (CAG) was performed for all patients prior to CABG. It was identified that 34 of the patients had left main artery (LM) lesions (with a degree of stenosis > 70%), 56 had complete occlusion of the anterior descending branch (LAD), 32 had complete occlusion of the anterior descending branch and right coronary artery (RCA), and 45 had diffuse lesions of three vessels with small vessels. Pre-operative echocardiography showed that the left ventricular ejection fraction (LVEF) was more than 45%, with an average of 51%. The range of left ventricular end-diastolic diameters (LVDD) was 48-67 mm, with an average of (58.3 ± 4.2) mm. Pre-operative electrocardiograms showed acute myocardial infarction in 27 patients, old myocardial infarction in 72 patients, and myocardial ischemia in 29 patients. The electrocardiogram was normal in 5 patients.

Inclusion criteria: (1) acute or old myocardial infarction; (2) LVEF ≥ 45%; (3) CAG showed a single or multiple lesions of the coronary artery with a stenosis rate > 70%, or occlusion; (4) sinus rhythm before and after operation; (5) patient signed informed consent form.

Exclusion criteria: (1) had received coronary artery stent implantation; (2) severe heart failure, LVEF < 40%; (3) non-sinus rhythm; (4) valvular disease, congenital heart disease, renal insufficiency, left ventricular hypertrophy, or various cardiomyopathies; (6) had received thrombolytic therapy during hospitalization; (7) autoimmune diseases or other diseases; (8) severe diseases.

This study was approved by the Ethics Committee of the First People's Hospital of Lanzhou.

Instruments and Methods

A Philips iE33, GE Vivid E9, and GE Vivid E95 color Doppler ultrasound machine (Netherlands) from the Functional Test Department of the First People's Hospital of Lanzhou was used, and the probe frequency was set to 2.5-5.0 MHz. Patients who received CABG were examined by echocardiography 1 month and 6 months post-operation. All patients were placed lying on their left sides, and the probe was placed on the chest. The observation was conducted on the apical four-chamber (A4C) view, and the transmitral peak flow velocity (E) was measured. The sampling line was then placed on the interventricular septal side of the mitral annulus and the lateral wall of the left ventricle, and the peak early diastolic velocity of the mitral annulus (Ea) was measured using TDI. Each index was measured for 3-5 cardiac cycles. The values were averaged, and the E/Ea ratio was calculated.

Sample Collection and Detection Methods

Serum, lithium heparin, heparin ammonia, and K2K3-EDTA plasma were collected using a standard sample collection tube containing separate glue. The samples were stabilized at 20-25°C for 3 days, at 2-8°C for 6 days, and at –20°C for 24 months. Before detection, samples that contained sediment were centrifuged, and it was ensured that all samples, calibration fluids, and controls were stored at an ambient temperature of 20-25°C.

The Roche full automatic electrochemiluminescence immunoassay system, Modular Analytics E170, Cobas e601, and Cobas e602

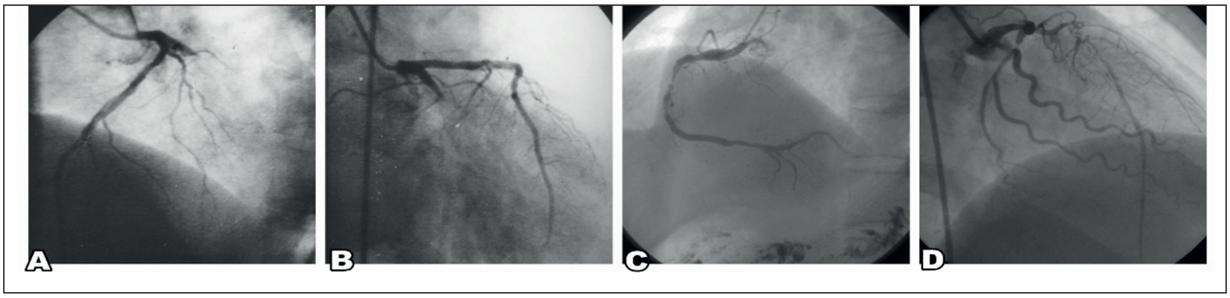

Figure 1. Coronary angiography. **(A)** Anterior descending branch occlusion; **(B)** circumflex branch occlusion; **(C)** multiple stenosis of right coronary artery; **(D)** multi-vessel stenosis of coronary artery.

analyzer were used. Due to the possibility of evaporation, the samples, calibration fluids, and controls loaded into the analyzer were tested within two hours. In order to obtain the best testing performance, the analyzer application instructions were followed. The analyzer automatically calculated the concentrations of the analytes in each sample (pmol/L or pg/mL) (1 pmol/L × 8.457 = 1 pg/mL, 1 pg/mL × 0.118 = 1 pmol/L).

Statistical Analysis

Statistical analysis was conducted using SPSS 18.0. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm SD$). Comparisons between two groups were conducted using a *t* test, and comparisons between multiple groups were conducted using analysis of variance (ANOVA). The correlation between each TDI index and NT-proBNP concentration was analyzed using multiple linear regression analysis, followed by Spearman's correlation analysis. Multivariate logistic regression analysis revealed a correlation between TDI index and NT-proBNP concentration pre-operation, 1 month post-operation, and 3-6 months post-operation. $p < 0.05$ was considered statistically significant.

Results

Surgical Outcomes

A total of 133 patients underwent CABG. Among these patients, internal mammary artery and great saphenous vein as bridging vessels. A total of 60 patients received grafting at one branch of the coronary artery, 43 received grafting at two branches of the coronary artery, and 30 received grafting at three branches of the coronary artery. Sadly, 2 of the patients subsequently died. In the surviving 131 patients, however, no evident complications were found during or after the operation. All patients underwent color Doppler examinations one month after the operation. However, only 121 patients were reviewed 3-6 months post-operation, as the other 10 were lost to follow-up (see Figures 1-3). The data of all examined patients were obtained by TDI, and the concentration of NT-proBNP in their blood was measured.

Analysis of Data Acquired Pre-Operation, 1 Month Post-Operation, and 3-6 Months Post-Operation

The data obtained pre-operation, 1 month post-operation, and 3-6 months post-operation (see Table I) were compared using univariate

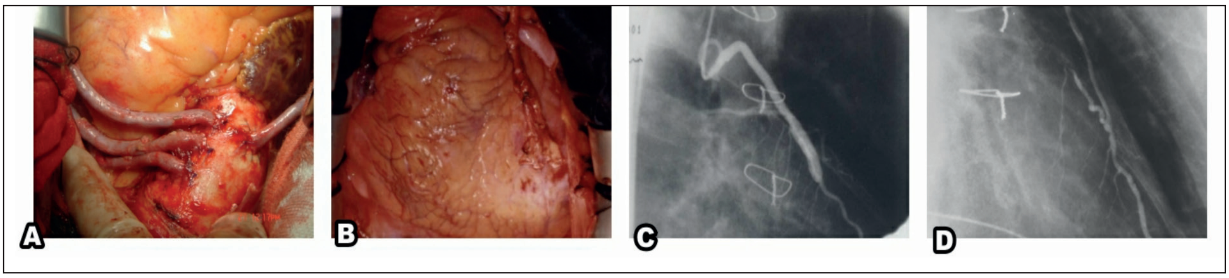

Figure 2. **(A + B)** Internal mammary vein and internal mammary artery bridge vessels; **(C + D)** Coronary angiography demonstrating venous and arterial bridging vessels.

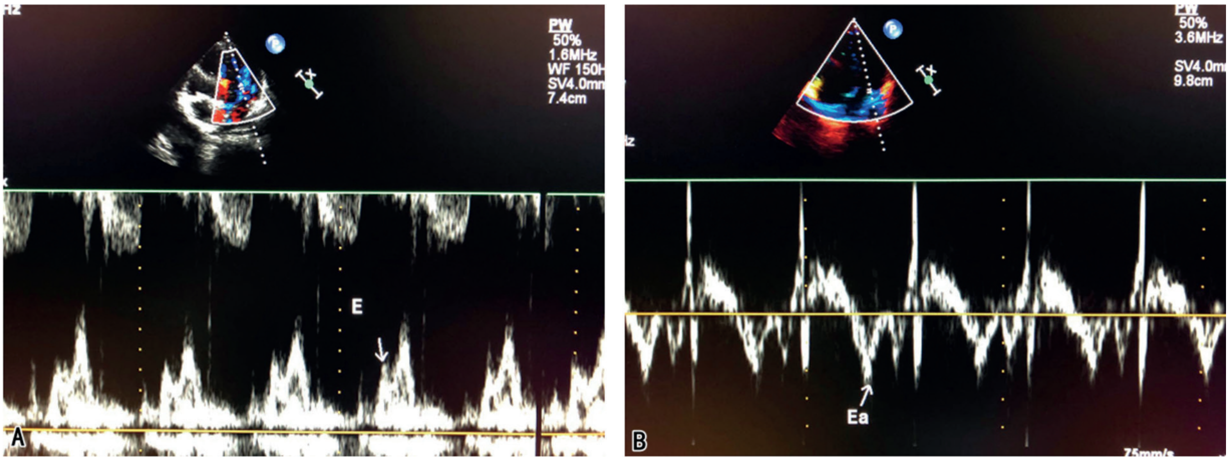

Figure 3. Echocardiographic reexamination of post-operation **(A)** measurement of mitral valve E peak velocity by Doppler spectrum; **(B)** TDI measurement of Ea value of mitral annulus.

Table I. Descriptive statistics.

	Pre-operation	1 month post-operation	3-6 months post-operation
BNP	2145.06 ± 959.37	1024.88 ± 612.69	630.42 ± 437.89
E/Ea	11.50 ± 3.39	10.36 ± 3.25	9.01 ± 3.44
Ea	3.94 ± 1.28	6.82 ± 2.02	8.42 ± 2.56
E	42.56 ± 9.11	66.04 ± 16.72	70.21 ± 18.07
N	133	13	121

ANOVA. $p < 0.05$ was considered statistically significant (see Table II). The E values, Ea values, and E/Ea ratios were analyzed using multiple linear regression analysis and a correlation between them and NT-proBNP concentration was examined using Spearman's correlation analysis. The correlations between the TDI index and NT-proBNP concentration are shown in Table III. The statistical data revealed a correlation between the E/Ea ratios obtained pre-operation, 1 month post-operation, and 3-6 months post-operation and the concentration of NT-proBNP. The differences were statistically significant (R = 0.489, 0.427, 0.557, respectively; $p < 0.001$). Furthermore, a correlation was found between Ea and the concentration of NT-proBNP at all three-time points, and the difference was statistically significant (R = –0.476, –0.479, –0.426, respectively; $p < 0.001$). However, no correlation was found between E and the concentration of NT-proBNP, and the difference was not statistically significant (R = –0.113, 0.161, 0.159, respectively; $p = 0.284$, 0.126, 0.164, respectively).

The results of the multivariate linear regression correlation analysis are shown in Figures 4-6. Figure 4 presents the correlation analysis between pre-operative NT-proBNP concentrations and the E/Ea ratios, Ea values, and E values pre-operation. Figure 5 presents this correlation analysis at 1 month post-operation, and Figure 6 presents it at 3-6 months post-operation.

Table II. Numerical analysis results of TDI – pre-operation and post-operation.

Check time	Number of cases	E (cm/s)	Ea (cm/s)	E/Ea
Pre-operation	133	42.83 ± 8.60	3.78 ± 1.42	11.71 ± 3.36
1 month post-operation	131	67.54 ± 16.25	6.85 ± 2.08	10.51 ± 3.42
3-6 months post-operation	121	71.23 ± 17.62	8.46 ± 2.76	9.02 ± 3.59
p		< 0.05	< 0.01	< 0.01

Table III. Correlation between NT-proBNP and the parameters of TDI using Spearman's correlation analysis at different time points.

	NT-proBNP	E/Ea	Ea	E
Pre-operation NT-proBNP R	1	.489	–.476	–.113
Significant (bilateral)		.000	.000	
N	133	133	133	133
1 month post-operation NT-proBNP R	1	.427	–.479	.161
Significant (bilateral)		.000	.000	.126
N	131	131	131	131
3-6 months post-operation NT-proBNP R	1	.557	–.426	.159
Significant (bilateral)		.000	.000	.164
N	121	121	121	121

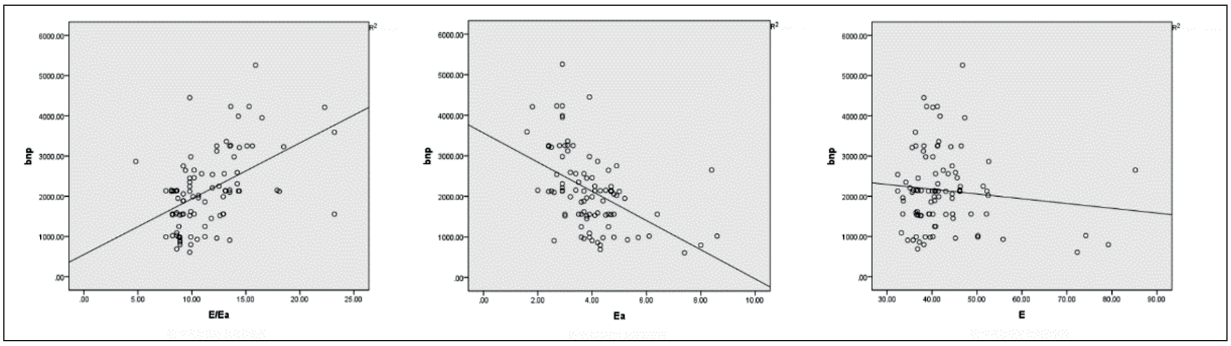

Figure 4. The correlation between pre-operative NT-proBNP concentration and E/Ea ratio, Ea value, and E value.

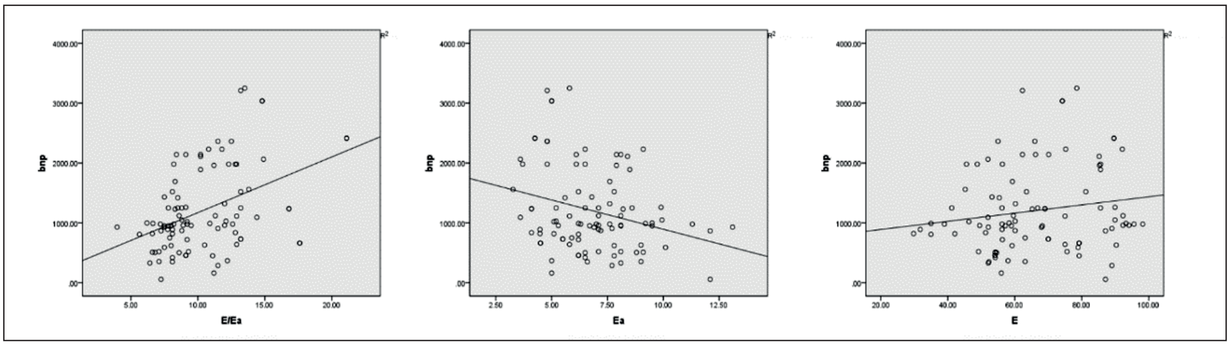

Figure 5. The correlation between NT-proBNP concentration and E/Ea ratio, Ea value, and E value 1 month post-operation.

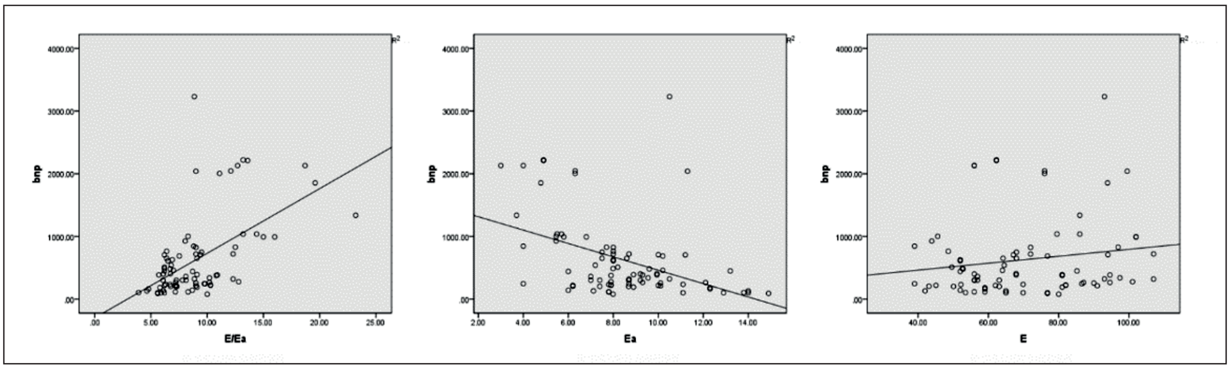

Figure 6. The correlation between NT-proBNP concentration and E/Ea ratio, Ea value, and E value 3-6 months post-operation.

Discussion

Ventricular diastolic dysfunction was first reported by Dougherty et al[13] in 1984, and clinicians have gradually improved their understanding of it with the accumulation of clinical data, making it a commonly identified independent disease in clinical practice and a well-studied one in clinical research. In the past, the assessment of ventricular diastolic function mainly relied on Doppler echocardiography, i.e., the indirect assessment of ventricular filling by measuring the velocity of blood flow across the mitral valve and the ratio of pressure difference (E/A). This index has high sensitivity to, and great diagnostic value for, early mild diastolic dysfunction. In the diagnosis of middle and late diastolic heart failure, there are possibilities of false normalization and super-normalization, which reduce the specificity and application value of diagnosis.

However, TDI can be used as a non-invasive examination method in clinical practice and can more quickly and accurately evaluate the recovery of ventricular diastolic function. It is not affected by gender, heart rate, two-dimensional image parameters, or LVEF. TDI can also measure Ea values in response to ventricular diastolic function, and it is not affected by preload.

Early diastolic Ea values are sensitive indicators of ventricular diastolic function[14-15], and studies have shown that there is a good correlation between early diastolic Ea value and left ventricular diastolic function grading. Ea values also reflect early mitral annular motion velocity in multi-sectional and multi-locus diastolic, so they can be used as a new index for estimating left ventricular filling pressure and pulmonary capillary wedge pressure (PCWP) and in the prognosis of many heart diseases, such as myocardial infarction and heart failure[17-18]. A normal E/Ea ratio is less than 8, with a ratio of 8-15 indicating impaired cardiac function and a ratio higher than 15 indicating a severely impaired index of cardiac function.

In thus study, echocardiography was carried out on the 121 patients who completed the study 1 month post-operation and 3-6 months post-operation. Their Ea values were measured at the interventricular septal side of the mitral annulus for 3-5 consecutive cardiac cycles using TDI, and the mean values were calculated. Their E values were also measured for 3-5 consecutive cardiac cycles, and the mean values were calculated. Their E/Ea ratios were then calculated.

NT-proBNP is a cardiac neurohormone secreted responsively from the ventricle during increased blood volume and pressure load. The elevation of NT-proBNP can reflect the elevation of left ventricular end-diastolic pressure, and the heart failure caused by systolic dysfunction or decreased diastolic function is usually accompanied by this elevation. The clinical information and imaging methods used in the past to diagnose left ventricular diastolic dysfunction have proved the significance of NT-proBNP in the control of cardiovascular diseases[19-20]. The concentration of NT-proBNP in serum and plasma is related to the prognosis of left ventricular dysfunction. After myocardial infarction, it is related to infarct size. Therefore, the determination of plasma NT-proBNP is a simple, accurate, and useful biochemical index for predicting the process of left ventricular remodeling after myocardial infarction. When NT-proBNP < 400 ng/L, the possibility of heart failure is very small. When NT-proBNP > 1500 ng/L, the possibility of heart failure is very high. If this marker continues to rise in clinical course, it suggests a poor prognosis[21-22].

In the present study, the improvement of left ventricular diastolic function after CABG was observed. The examination results 1 month post-operation revealed that left ventricular diastolic function had improved and E/Ea ratios and NT-proBNP concentrations had decreased. During examination 3-6 months post-operation, it was observed that left ventricular diastolic function had further improved, Ea values had increased, and E/Ea ratios had decreased. This suggests that left ventricular filling pressure had decreased, left ventricular systolic function had further improved, and NT-proBNP concentration had further decreased.

Conclusions

A linear correlation was identified between TDI parameters (Ea, E/Ea) and NT-proBNP concentration at different time points of left ventricular diastolic function recovery after CABG ($p < 0.01$), but there was no significant correlation between mitral E peak velocity as measured by spectral Doppler and NT-proBNP concentration.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki and with approval from the Ethics Committee of the First People's Hospital of Lanzhou. Written informed consent was obtained from all participants.

Funding

Foundation Project: Gansu Science and Technology Program Subsidized Project (17YF1FA138).

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