**Introduction**

Pheochromocytoma was a kind of neuroendocrine tumor. Due to tumor, paroxysmal or persistent catecholamine (CA) secreted which resulted in blood pressure abnormalities and metabolic disorders. Clinical manifestations were episodic hypertension (0.1% to 0.6% of patients with hypertension) and triads: headache (80%), hyperhidrosis (63%), palpitation (60%). Some patients had severe heart, brain, kidney damage or hypertensive crisis due to long-term hypertension. Patient survival rate was exclusively 50% after surgery without clear preoperative diagnosis. This may made the doctors miss the opportunity for taking effective preventive measures such as controlling blood pressure, correcting arrhythmia and expanding to protect patients with pheochromocytoma.

Traditional biochemical indicators for the diagnosis of pheochromocytoma included blood CA, urinary CA, urinary vanillylmandelic acid, and so on which was lack of sensitivity and specificity.

Latest research suggested that compared with other biological indicators, the catecholamine metabolite group Metanephrines (MNs) including Metanephrine (MN), Normetanephrine (NMN), (3-Methoxytyramine, 3-MT) had a great value for the auxiliary diagnosis of pheochromocytoma. (Fig.1)

**Method Development**

A Waters® Xevo™ TQ MS ACQUITY UPLC® System was used to develop the detection method. We developed and optimized a Liquid chromatography-tandem mass spectrometry (LC-MS/MS) based MNs quantification method (Fig.2). The signal linearity, lower limits of quantitation, precision, accuracy and stability of LC-MS/MS has been evaluated. On the basis of the completion of performance verification, follow-up research was carried out to establish a reference range and cutoff value for MNs detection which would provide a clinical diagnosis strategy for pheochromocytoma and paraneoplastic.

**Clinical Application**

LC-MS/MS based MNs detection was applied to pheochromocytoma diagnosis in Zhongshan Hospital since 2011. More than 17k test were detected in 2018.

**Conclusion**

We developed a high throughput, high sensitivity and high specificity LC-MS/MS based MNs quantification method. We established a clinical reference range from 255 normal people and screened out the cutoff value through large-scale clinical validation with 1262 disease samples and 500 normal samples. This study provided a clinical diagnostic strategy for pheochromocytoma.