The 722nd Kitasato Medical Society Invitational Academic Lecture Series Abstract

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Mechanical circulatory support and ventilatory support of cardiac patients

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As cardiothoracic anesthesiologists, we are continuously involved in the care of patients undergoing the most advanced care－patients who require mechanical circulatory and ventilatory support. Our expertise is expanded into 2 areas－the operating room (OR) and the intensive care unit (ICU). In the operating room we participate in decisions－when and if we should apply support, and what kind of support is the most appropriate for a given clinical situation. In the ICU, we need to adjust parameters of support, and at the same time establish the delicate balance between bleeding and risk of thrombosis. The aim of this presentation is to discuss the indications and all aspects of perioperative care of patients who require advanced mechanical circulatory or respiratory support.

There are 3 types of indications for elective mechanical circulatory support in the OR. First is elective surgery when a left ventricular assist device (LVAD) is placed as a bridge to recovery, a bridge to heart transplantation, or a bridge to destination. These indications should be discussed among all members of the team involved in care of these patients. There are several LVAD devices available on the market but recent research is clearly indicating that a fully magnetically levitated pump offers the lowest complications. The are many challenges facing anesthesiologist managing these cases. Among the most important ones are right ventricular dysfunction and bleeding. Use of mechanical circulatory support for urgent treatment (cardiogenic shock) is much more controversial, and we are currently lacking convincing evidence. Among the devices used, we should mention the intra-aortic balloon pump (IABP), the Impella pump, the Centrimag pump, and the Veno-Arterial ECMO. Definitely, evidence for IABP and Impella pump is negative, and the other devices need more evidence.

Discussion regarding respiratory support is dominated by the use of veno-venous ECMO. Recent years have seen an exponential increase of its use all over the word. Advances in technology, miniaturisation and decreased requirements for anticoagulation facilitated spread of this therapy. At the same time, recent results of the EOLIA trail revigorated ongoing discussion on indications and appropriateness of the VV ECMO use. There is no question that this is the only option for treatment of patients with acute respiratory failure not responding to any other therapies. On the other hand, its complexity and level of expertise requires establishment of referral centers, which can offer necessary resources and capability to offer state-of-the-art care.

The aforementioned modes of treatment of patients requiring advanced mechanical circulatory and respiratory support need high-end critical care service, which is the natural extension of services provided in the OR. The basic requirements of such therapy require minimal annual case loads, 24-h availability of transesophageal echocardiography, and point-of-care diagnosis of excessive bleeding or hypercoagulability. The level of expertise (annual case load) seems to be crucial for a good outcome of these high-risk patients.

The 724th Kitasato Medical Society Invitational Academic Lecture Series Abstract

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The beneficial effect and mechanism of QiShenYiQi Pills on ischemia/reperfusion induced myocardial injury and fibrosis in rats

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Thrombolytic therapy and/or percutaneous coronary intervention may lead to myocardial ischemia and reperfusion (I/R) injury, which further develops to myocardial fibrosis, and finally heart failure. Myocardial I/R injury, resulted from recanalization of the occluded vessels, is a complicated pathological condition including abnormal energy metabolism, oxidative stress, inflammatory factors and apoptosis. Ribosomal protein S19 (RP S19), released after myocardial injury, induces monocyte infiltration and macrophage polarization towards M2. M2 macrophages secrete transforming growth factor β1 (TGFβ1), which acts on fibroblast TGFβ receptor II (TGFRβRII), activates Smad system, and leads to collagen deposition and myocardial fibrosis. However, at present, drugs recommended by the guidelines are not able to block myocardial I/R injury and fibrosis.

QiShenYiQi Pills (QSYQ), consisting of Radix Astragalus, Salvia miltiorrhiza Bunge, Panax notoginseng and Dalbergia odorifera, is a compound Chinese medicine (Registration NO.: Z20030139), which is adopted by expert consensus on the prevention and treatment of chronic heart failure by combining traditional Chinese medicine with western medicine. Our work demonstrated that pre-treatment with QSYQ improved myocardial energy metabolism and ameliorated myocardial injury during the ischemia period. It also reduced myocardial infarction area and apoptosis and improved myocardial blood flow. On the other hand, post-treatment with QSYQ inhibited myocardial fibrosis, improved cardiac function and increased myocardial blood flow after I/R, which was related to inhibiting RP S19 release, monocyte infiltration, macrophage polarization towards M2, TGFβ1 release, Smad activation and collagen deposition. Our *in vitro* study demonstrated that QSYQ reduced C5aR protein expression and C5aR-RP S19 co-localization in monocytes and TGFβRII expression and P-Smad3 translocation from cytoplasm to nuclei in fibroblasts.

In the seminar, the speaker will systematically introduce the mechanism underlying myocardial injury and myocardial fibrosis induced by I/R, as well as the beneficial effect and possible mechanism of QSYQ on myocardial injury and fibrosis.

The 726th Kitasato Medical Society Invitational Academic Lecture Series Abstract

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Stereotactic body radiotherapy (SBRT) for renal cell carcinoma RCC: from overcoming radio-resistance to enhanced abscopal effect

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Renal cell carcinoma (RCC) is traditionally believed to be radio-resistant. The role of radiotherapy in the management of primary and metastatic RCC is mainly for symptoms palliation as previous clinical trials showed no overall survival benefits. Stereotactic radiosurgery (SRS)/Stereotactic body radiation therapy (SBRT) developed as a result of technological advances in image-guidance radiotherapy (IGRT), treatment planning, brain/body stereotaxis and motion management, allows precise delivery of biologically potent or ablative dose to the tumor targets. Preclinical and clinical studies of SRS/SBRT have now demonstrated excellent tumor control without significant toxicity in the treatment of primary RCC as well as intracranial and extracranial metastatic RCC lesions. The additional benefit of SRS/ SBRT is the abscopal (distant bystander) effect, mediated by immunological response. In addition, ablative-high-dose radiation such as SRS/ SBRT may overcome radio-resistance of RCC caused by the von Hippel Lindau (VHL) tumor suppressor gene mutation and hypoxia-inducible factor-1 (HIF-1). Pathological evidence of complete response after high-dose-focused SRS/SBRT will be presented. The past (low-dose radiotherapy), present (high dose SRS/SBRT) and future (combined radiotherapy/SRS/SBRT with immunotherapy) of abscopal effects of radiotherapy will be illustrated and discussed. The proposed mechanisms of action of abscopal effect of radiotherapy/SRS/SBRT will be presented. The most exciting aspect of combined immunotherapy and radiotherapy/SRS/SBRT (iSRS/iSBRT) is the enhanced abscopal effects seen in many tumor types and the potential to impact positively on local control and may be survival in patients with oligometastases. Single institutional to multi-institutional studies and promising, efficacious outcomes of International Radiosurgery Oncology Consortium for Kidney (IROCK) will be highlighted. Our own pattern of care study of National Cancer Database (NCDB) will also be presented. As radiotherapy is not considered as definitive treatment of RCC, combination of radiotherapy and various systemic therapies has not been examined previously. However, SRS/ SBRT could change the role of radiotherapy for RCC, and development of combination therapy including immunotherapy and targeted therapy needs to be explored in the future trials. Challenges and future directions of iSRS/iSBRT will also be discussed including biomarkers, tumor response evaluation and treatment related toxicity. Radiotherapy for RCC, although once an overlooked treatment approach, is now undergoing a renaissance and moving towards the forefront of RCC management.