

REVIEW *The Centenary Commitment to Improving Healthcare by the Communist Party of China*

Anesthesia Management at Fuwai Hospital: Practice, Evidence and Outcomes

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Key words: Anesthesia; management; cardiac surgery; outcome

Abstract Fuwai Hospital was established in 1956 and the Anesthesia Department of Fuwai Hospital was one of the earliest anesthesia departments then in China. Under the leadership of several department directors and with the concerted efforts of all generations of colleagues, the Anesthesia Department of Fuwai Hospital has dramatically transformed, upgraded and modernized. For more than six decades, the Anesthesia Department has been providing high-quality peri-operative anesthesia care for cardiovascular surgeries, conducting innovative experimental and clinical researches, and offering comprehensive training on cardiovascular anesthesiology for professionals across China. Currently, Fuwai Hospital is the National Center for Cardiovascular Diseases of China and one of the largest cardiovascular centers in the world. The present review introduces the Anesthesia Department of Fuwai Hospital, summarizes its current practice of anesthesia management, the outcomes of cardiovascular surgeries at Fuwai Hospital, accumulates relevant evidence, and provides prospects for future development of cardiovascular anesthesiology.

FUWAI Hospital was established in 1956 after the founding of the People's Republic of China. For more than six decades, Chinese pioneers in cardiovascular specialty at Fuwai Hospital have been dedicated to improving care of cardiovascular diseases. Currently, Fuwai Hospital serves as the National Center for Cardiovascular Diseases (NCCD) of China, and is one of the largest cardiovascular medical centers in the world.^[1] The Anesthesia Department at Fuwai Hospital has been improving and

developing continuously. With the efforts of several generations of departmental leaders and all their colleagues, the department provides high-quality peri-operative care, which serves for the large volume cardiovascular surgeries at Fuwai Hospital as a professional and stable support.

GENERAL INTRODUCTION

I. Department leaders and faculties

During the first decade since the People's Republic of China was founded, there were few anesthesia departments in China. The outstanding leaderships by the chairs of the Anesthesia Department at Fuwai Hospital have played important roles in the departmental development since it was founded in 1956.

Received May 5, 2021; accepted May 24, 2021; published online August 18, 2021.

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Professor Deyan Shang (1918-1985), the first Chairperson of the department, is one of the pioneer anesthesiologists in China. He received his medical training during 1947-1949 at the American Hospital, University of Illinois College of Medicine in Chicago.^[2] For his groundbreaking works with his colleagues, the "Beijing Code One", a domestic-made cardiopulmonary bypass (CPB) machine, was successfully developed at Fuwai Hospital in 1958, and the first on-pump intracardiac surgery was successfully performed under hypothermic anesthesia at Fuwai Hospital in 1959. Professor Shang was the founder of Chinese cardiac anesthesiology. He also served as the first president of the Chinese Society of Anesthesiology (CSA) in 1979 and the deputy chief editor of the *Chinese Journal of Anesthesiology* which was launched in 1981.^[2]

Professor Shouchun Xu (1927-), the second department Chair, graduated from Peking Union Medical College in 1954 and started his career at Fuwai Hospital in 1956. Professor Xu has made great contribution to the research and development of domestic-made CPB machines, CPB associated coagulopathy mechanism and management, and also committed a lot to the resident training for anesthetists, etc.

Professor Xiaoqin Hu (1932-), the third department Chair, performed the first on-pump intracardiac surgery for newborn patients in China in 1989 together with her colleagues. She initiated experimental and clinical research on extracorporeal membrane oxygenation (ECMO) in China early in 1990s. To adapt to the increasing surgical volume at Fuwai Hospital, professor Hu established the first CPB department in China in 1994.

Professor Jin Liu (1956-), the fourth department Chair till 2000, was the 11th president of the CSA. He also served as the first president of the Chinese Anesthesiologists Association (CAA) and the first president of the National Society of Cardiovascular Anesthesia (NSCVA). Since 2000, Professor Liu continued his leadership in the Anesthesia Department at West China Hospital, Sichuan University. He devotes his professional career mainly to anesthesia residency program, echocardiography training, blood conservation, and new drug development.

Professor Lihuan Li (1950-), the fifth department Chair, is a renowned cardiac anesthesiologist and the former head of Cardiovascular Anesthesia Subspeciality of CSA. He has been dedicated to the experimental research and clinical translation of myocardial protection,

patient blood management, etc. In 2005, he initiated to establish the International Chinese Cardiovascular Anesthesia Form (ICCAF), which is held annually thereafter, and promotes professional communication and cooperation in the field of cardiovascular anesthesia. Professor Li served as the first president of the Chinese Society of Cardiothoracic and Vascular Anesthesiology (CSCVA), which was founded in Beijing in 2015.

Professor Fuxia Yan (1965-), the sixth and current department chair, is expertized in pediatric cardiac anesthesia. Presently, she acts as the head of Pediatric Cardiac Anesthesia Subspecialty of CSCVA. She has made great achievement in the fields of anesthesia management of cardiac surgical newborns, pediatrics with complexed cardiovascular anomaly, enhanced recovery after cardiac surgery of pediatric patients, pulmonary protection, etc.

Under the leadership of several generations of chairs, with the concerted efforts of all colleagues in the past six decades, the Anesthesia Department at Fuwai Hospital has dramatically transformed, upgraded, and modernized, which can be reflected from the developing milestones (**Table S1**) and the equipment/device overview (**Table S2**) of the department. Besides providing high-quality peri-operative clinical care, faculties in the Anesthesia Department also conduct multiple clinical research and innovative experiments, offer comprehensive post-graduate education and training opportunities for cardiovascular anesthesiologists. Currently, there are 52 physicians in the department, including 45 anesthesiologists, 6 residents, 1 echocardiography physician, and 2 departmental secretaries. The age and gender distributions of the faculties are presented in **Figure 1**. The research of department covers the areas of organ protection, blood conservation, cognitive dysfunction, evidence-based medicine, etc. In 2019, there were 20 publications on Web of Science indexed journals. The enrollment of cardiovascular anesthesia fellow physicians and anesthesia master students at Fuwai Hospital can be dated back to 1956 and 1992, respectively. Currently, there are three doctoral supervisors and four master's supervisors in the department. Annually, 40-60 fellow doctors from hospitals around China receive half or one year specialty training on cardiovascular anesthesia at Fuwai Hospital.

II. Anesthesia service and workload

Anesthesiologists at Fuwai Hospital provide anesthesia

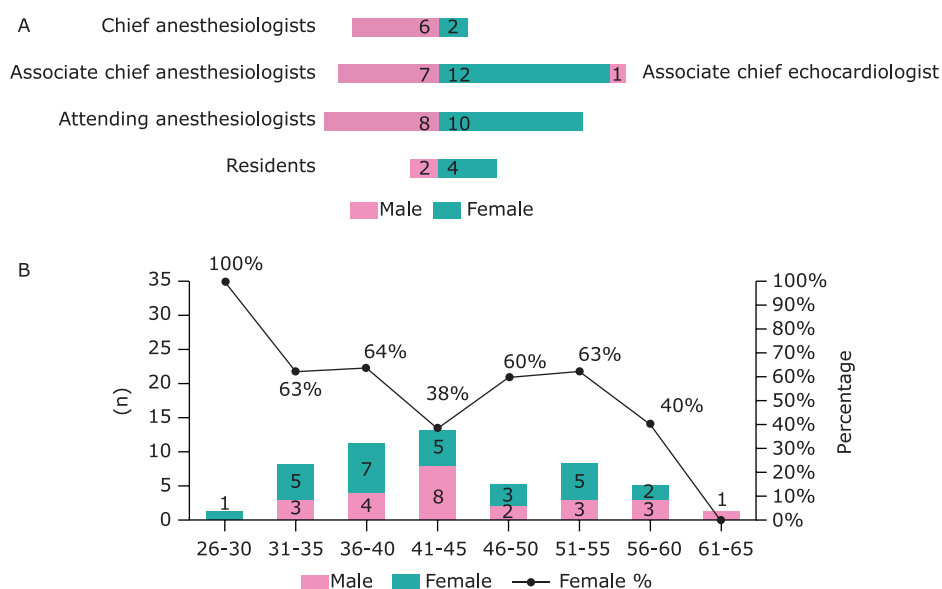


Figure 1. Age and gender distributions of faculties in the Anesthesia Department at Fuwai Hospital. Colors of green and pink represent the scrub colors of the female and male physicians.

care in various types of cardiovascular surgeries and interventional diagnostic and therapeutic procedures for adult and pediatric patients. They are also responsible for in-hospital procedures such as arterial and central venous lines insertion, endotracheal intubation, cardiopulmonary resuscitation, acute pain service, etc. Taking the year 2019 as an example (**Figure 2**), anesthesiologists at Fuwai Hospital provided perioperative care of elective or emergency cardiovascular surgeries for 14,808 patients in 26 operating rooms, and of car-

diac interventional or electrophysiological procedures for 2,590 patients in 17 catheterization laboratories.^[3] Additionally, anesthesia physicians performed 1,249 arterial catheterizations, 1,284 central venous catheterizations, 377 endotracheal intubations, and 300 acute pain service during shifts. Since 2018, anesthesiologists at Fuwai Hospital have undertaken the work of intraoperative transesophageal echocardiography (TEE) examination in cardiovascular surgeries for adult patients. By far, 14 anesthesiologists have fulfilled the

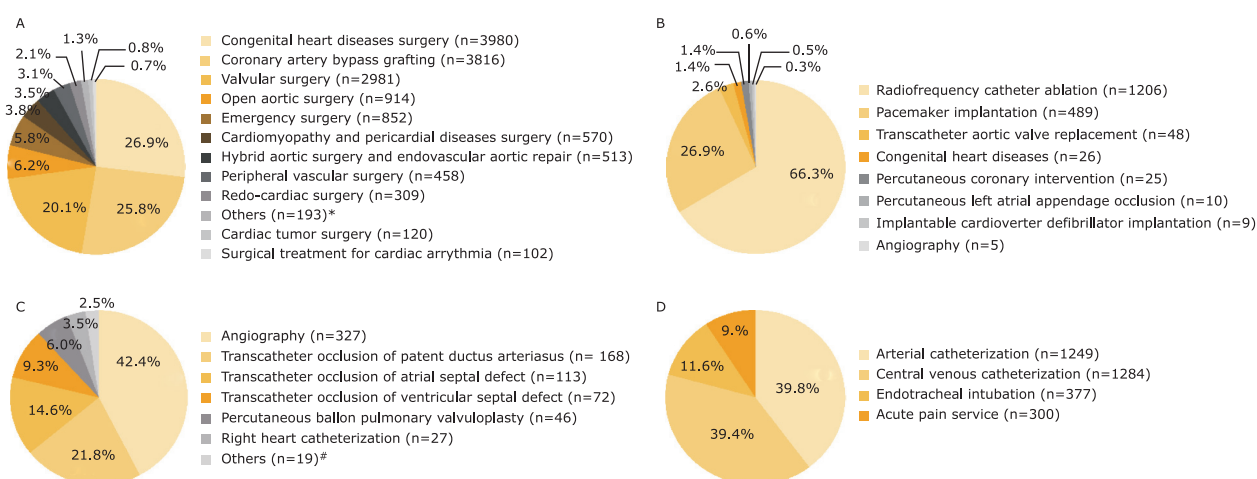


Figure 2. Anesthesia services and workload of the Anesthesia Department at Fuwai Hospital in 2019

(A) Cardiovascular surgery. (B) Adult interventional cardiac and electrophysiological procedures. (C) Pediatric interventional cardiac procedures. (D) Anesthesia service during shifts.

*including interventional cardiovascular surgery, ventricular assisted device implantation thrombectomy, and ventricular aneurysm surgery; #including balloon dilation procedures for lesions of aorta, pulmonary veins, and superior vena cava.

TEE training; in 2019, they performed intraoperative TEE examinations for 5,408 patients. With the anesthesia care, annual surgical volume at Fuwai Hospital has exceeded 10,000 cases since 2011, and the 30-day postoperative mortality rate has been below 1% for 12 consecutive years.^[3]

ANESTHESIA PRACTICE

I. Monitoring

1. Standardized monitoring

At Fuwai Hospital, standardized intraoperative monitoring for cardiovascular surgical patients includes electrocardiogram (ECG), pulse oximetry (SpO₂), capnography (ETCO₂), arterial blood pressure (ABP), central venous pressure (CVP), body temperatures, etc. Upon patient's arrival at operating room, oxygen is inhaled *via* face mask and SpO₂ is monitored. For ECG monitoring, 5- and 3-electrode systems are used for adults and pediatrics, respectively.

After 2% lidocaine infiltration, arterial catheterization for ABP monitoring is performed before anesthesia induction for adults and after anesthesia induction for pediatrics. Radial artery of the nondominant hand is the most frequent cannulation site, followed by brachial artery, femoral artery, dorsalis pedis artery, and axillary artery. After general anesthesia induction, central vein is cannulated with three-lumen central vein catheter (CVC). Internal jugular vein (IJV) is the most often used access route for CVC, followed by subclavian vein and femoral vein. Technique of ultrasound prelocation or real-time guidance is utilized for arterial and venous catheterization when necessary. At Fuwai Hospital, continuous pressure of 300 mmHg and a flow rate of 3 mL/h of heparinized saline (5 U/mL) flushing solution are routinely used to maintain arterial line and CVC patency perioperatively.

Nasopharyngeal and bladder temperatures are routinely monitored for adult patients, and nasopharyngeal and rectal temperatures for pediatric patients. Blood temperature is monitored in patients with pulmonary artery catheter *in situ*. Fluid infusion and blood transfusion warming devices, and forced-air heater are selectively utilized in complexed procedures (e.g., thoracoabdominal aortic aneurysm repair), newborn and low body weight pediatric surgeries, and lengthy operations.

2. Pulmonary artery catheter

Pulmonary artery catheter (PAC) is inserted for

the measurement of pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), continuous cardiac output (CCO), other hemodynamic variables (e.g., systemic and pulmonary vessel resistance), and oxygenation variables (e.g., mixed venous oxygen saturation). The insertion of PAC at Fuwai Hospital is patient- and procedure-indicated. For example, PAC is utilized in patients with impaired heart function or pulmonary hypertension at the discretion of anesthesiologists. For some surgical procedures (e.g., pulmonary endarterectomy, heart transplantation), PAC is routinely inserted.

In a retrospective analysis by Xu *et al.*^[4] which included 1,361 consecutive patients undergoing isolated and primary CABG at Fuwai Hospital, PAC was utilized in 453 patients and not in the other 908 patients. It demonstrated that, PAC use was neither associated with perioperative mortality or morbidities, nor was it associated with long-term mortality and major adverse cardiac and cerebrovascular events (MACCE), and that the patients with PAC more likely needed inotropic support [dopamine: 70.9% vs. 45.5%, $P < 0.001$; epinephrine: 7.7% vs. 2.6%, $P < 0.001$], and had higher hospitalization expenditure than those without PAC (\$14,535 vs. \$13,873, respectively, $P = 0.004$).^[4]

3. Left atrial pressure

Left atrial pressure (LAP) monitoring, which is useful in assessing left heart function, can be indirectly reflected by PCWP measured *via* PAC. But it is difficult to insert a PAC in pediatric patients with congenital intracardiac deformities. Therefore, inserting a LAP-monitoring catheter directly into left atria (LA) *via* various routes is a common method. For pediatric patients undergoing tetralogy of Fallot (TOF) reconstruction and surgical repair for congenital heart diseases complexed than TOF at Fuwai Hospital, a triple-lumen CVC plus a single-lumen CVC are routinely inserted after anesthesia induction. After repairing the primary intracardiac defects, the distal tip of the single-lumen catheter is passed into the LA by surgeon through an existing atrial septal defect (ASD) or an intra-atrial septal incision. ASD or the incision is then closed around the single-lumen catheter, and the catheter is fixed to intra-atrial septum by suturing to avoid accidental withdrawal of the catheter tip. After CPB, the triple-lumen catheter in the IJV and the single-lumen catheter in the LA are used to monitor CVP and LAP, respectively. Yan *et al.*^[5] from Fuwai Hospital invented a modified triple-lumen catheter that incor-

porates a single lumen microtube that can be placed in the left atrium intraoperatively, avoiding the traditional "double-stick" technique in IJV. The spiraled distal tip of the microtube reduces the chance of migration into right atrium (RA).

4. Transesophageal echocardiography

At Fuwai Hospital, ultrasound physicians have been traditionally responsible for the examination and interpretation of intraoperative TEE, even though there are several color Doppler flow imaging (CDFI)-qualified and TEE-trained anesthesiologists.^[6] Pre-CPB TEE allows to confirm a preoperative diagnosis, is therefore routinely performed after anesthesia induction in procedures like planned mitral and aortic valvuloplasty, extended myectomy for hypertrophic obstructive cardiomyopathy (Morrow procedure), surgery for complex congenital heart deformities, *etc.* Post-CPB TEE is performed in valvular surgery, Morrow procedure, congenital heart disease correction, heart transplantation, and other procedures when necessary. Since 2018, intraoperative TEE examinations for adult cardiovascular surgical patients have been taken over by anesthesiologists who had received at least 3 month of TEE training, and their TEE reports are verified and issued by an ultrasound physician. Thus, the intraoperative TEE has gradually become an integral part of anesthesiologists' daily work at Fuwai Hospital. With increasing use of TEE and more physicians trained, anesthesiologists are further involved in the decision-making processes (*e.g.*, confirmation of preoperative diagnosis, evaluation of surgical effectiveness) and outcome improvement.

5. Cerebral monitoring

Bispectral index (BIS), near infrared spectrum (NIRS) and transcranial Doppler (TCD) are currently available at Fuwai Hospital for central nervous system monitoring for different purposes, *e.g.*, BIS to determine optimal anesthesia depth, NIRS to monitor regional cerebral oxygenation, and TCD to measure cerebral blood flow velocity. At Fuwai Hospital, BIS is used in adult and pediatric cardiovascular surgical patients intraoperatively, especially when fast tracking anesthesia is planned. NIRS is routinely applied in procedures such as aortic arch repair, cervical endarterectomy (CEA), and pulmonary endarterectomy (PEA). TCD can be used to measure flow velocity of cerebral basilar arteries and detect embolic signals within these arteries. It is mainly utilized for research purpose at Fuwai Hospital.

II. Point-of-care tests

1. Coagulation tests

Activated clotting time (ACT) is routinely used to monitor heparinization and its reversal by protamine at Fuwai Hospital. ACT+ (Hemochron® Jr., USA) is used to monitor moderate to high levels (1-6 U/mL) of heparinization during cardiovascular surgery. ACT-LR (Hemochron® Jr., USA) and APTT (Hemochron® Jr., USA) are available for monitoring low to moderate levels of heparinization, which are frequently associated with procedures such as intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO), and hemodialysis. ACT-LR values are linearly correlated to the anticoagulation effects of low to moderate heparin concentration up to 2.5 U/mL. APTT test is used for evaluation of low dose heparinization (up to 1.5 U/mL). Thrombelastography (TEG) or rapid TEG (r-TEG) with platelet mapping test is used to monitor hemostasis defects, such as coagulation factor deficiency, hypofibrinogenemia, and platelet dysfunction.^[7,8]

2. Blood gas and chemistry analysis

Intraoperative blood gas and chemistry analyses are performed regularly at Fuwai Hospital. Blood for tests is sampled *via* arterial catheter or CVC by anesthesiologists pre- and post-CPB, and *via* CPB circuit by perfusionists during CPB. The blood gas variables measured and calculated include potential of hydrogen (pH) value, carbon dioxide tension (pCO₂), base excess (BE), bicarbonate (HCO₃⁻), oxygen saturation (SO₂), oxygen tension (PO₂), oxygen tension of hemoglobin half-saturation (P₅₀), oxygen capacity (O₂cap), oxygen content (O₂ct), respiratory index (RI), oxygen index (OI), alveolo-arterial oxygen tension difference (A-aDO₂), and arterial-alveolar oxygen tension ratio (PO₂-a/A). When PAC is in place, mixed venous oxygen saturation (SvO₂) can be continuously monitored on the screen after calibrating with the first SvO₂ value of blood sample *via* PAC. Blood chemistry variables include electrolytes sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺), magnesium (Mg²⁺) and chloride (Cl⁻) ions, hemoglobin (Hb), hematocrit (Hct), glucose (Glu), lactate (Lac), blood urea nitrogen (BUN) and osmole (Osm).

3. Colloid osmotic pressure

Plasma colloid osmotic pressure (COP) is an important factor controlling the balance of blood inside and outside the fluid vessels. It is common practice at Fuwai Hospital to maintain COP between 12-14 mmHg during CPB and 16-20 mmHg after CPB by means of

colloid priming and hemofiltration. For adults undergoing on-pump cardiac surgery at Fuwai Hospital, 6% hydroxyethyl starch 130/0.4 Voluven (Fresenius Kabi, Germany) 1,000 mL is added to the CPB prime.^[9] In recent years, the safety and efficacy of bloodless priming strategies have been scrutinized in pediatric patients at Fuwai Hospital. For example, Liu *et al.*^[10,11] investigated the safety and feasibility of substituting fresh frozen plasma (FFP) or human serum albumin (HSA) with 4% succinylated gelatin Gelofusine (Braun Medical, China) for CPB priming in cyanotic and non-cyanotic pediatrics who aged less than 3 years and weighted down to 5 kg.

4. Free hemoglobin

Free hemoglobin (fHb) releasing into plasma during destruction of red blood cells or hemolysis is a common phenomenon in patients undergoing cardiovascular surgeries. The pathogenesis of hemolysis in cardiovascular surgical patients may include but is not limited to preexisting defects, mechanical trauma, inappropriate osmotic pressure, free radical stress, complement activation, *etc.* Hemolysis in cardiovascular surgical patients is associated with increased consumption of intravascular nitric oxide and perioperative damage of kidney and intestinal tissue. At Fuwai Hospital, fHb concentration is regularly monitored during extracorporeal circulating procedures [*e.g.*, CPB, ECMO, ventricular assist device (VAD)], or when indicated.

III. Anesthetic premedication, induction and maintenance

1. Premedication

Chronic cardiac medications (*e.g.*, anti-hypertensive, anti-anginal agents) are continued in patients till the morning of surgery. Anesthetic premedication varies greatly among anesthesiologists. Some anesthesiologists prescribe oral intake of midazolam 7.5 mg, metoprolol 6.25 mg and diltiazem 15 mg plus intramuscular injection of morphine 10 mg for patients on the day of surgery. Some anesthesiologists prescribe oral intake of diazepam 10 mg and ranitidine 0.3 g. Other anesthesiologists prescribe no anesthetic premedication.

2. Anesthetic induction

For adults, general anesthesia is induced with intravenous etomidate / propofol, midazolam and sufentanil / fentanyl (**Table S3**). Endotracheal intubation is facilitated with muscular relaxant cisatracurium. Penehyclidine hydrochloride (PHC), a new generation of

anticholinergic drug with less unwanted cardiovascular effects (*e.g.*, tachycardia), is widely used as anesthetic premedication in China. PHC is administered during induction in pediatric and adult patients by some anesthesiologists at Fuwai Hospital.

3. Anesthetic maintenance

After ETT intubation and CVC placement, anesthesia is maintained with either total intravenous anesthesia (TIVA) *via* CVC, or combined inhalational (sevoflurane) and intravenous anesthesia (**Table S3**). Adequate anesthesia depth is achieved by maintaining BIS value between 40-60 intraoperatively.

4. Inotropic and vasoactive drugs

At Fuwai Hospital, administration of inotropic or/and vasoactive medications are typically started in operating room at discretion of both the attending anesthesiologist and the cardiac surgeon based on patient characteristics, cardiovascular lesions, and physiological status. For CPB procedure, intravenous infusion of inotropic or/and vasoactive medications *via* electronic infusion pumps are initiated upon rewarming during CPB and continued postoperatively. After arrival at the surgical intensive care unit (SICU) postoperatively, the inotropic or/and vasoactive medications for patient (**Table S3**) are mainly adjusted by intensivists. Inotropes for continuous intravenous infusion include dopamine, dobutamine, milrinone, epinephrine, levosimendan, *etc.*^[12-18] Vasopressors for continuous intravenous infusion mainly include norepinephrine, methoxamine, vasopressin,^[19] and vasodilators of choice mainly include nitroglycerin, isosorbide dinitrate, nitroprusside, nicardipine, urapidil. Jia *et al.*^[12] retrospectively analyzed 186 children undergoing surgical repair of TOF at Fuwai Hospital, who were divided into 2 groups, namely epinephrine or dopamine-dobutamine mixture, according to their intraoperative inotropes. They demonstrated that epinephrine was neither associated with superior hemodynamics nor with improved short-term outcomes as compared to dopamine- dobutamine mixture. In a RCT study on 67 CABG patients with triple-vessel coronary artery disease and impaired left ventricular function (LVEF<40%), Chen *et al.*^[15] demonstrated that postoperative administration of levosimendan remarkably improved heart function (lower SVR, CVP, and increased CO) and reduced the incidence of adverse events (prolonged mechanical ventilation, atrial fibrillation, acute kidney injury). Lu *et al.*^[19] evaluated the efficacy of vasopressin in

managing post-cardiotomy vasodilatory shock with 70 consecutive pediatrics and demonstrated that vasopressin administered continuously at a rate range of 2×10^{-4} – 20×10^{-4} U/kg/min significantly improved hemodynamics, decreased vasopressor requirement, and increased urine output without significant adverse effects.

IV. Airway management

1. Endotracheal intubation

At Fuwai Hospital, UEScope (UE Medical Co., China), a video laryngoscope with disposable angulated blades or reusable Miller blades, is most often used for intraoperative endotracheal intubation (ETT) in adult and pediatric patients and ETT outside operating room (e.g., for cardiopulmonary resuscitation). Cuffed single lumen tubes (SLT) of size 7.0/7.5 and size 7.5/8.0 with disposable stylets are respectively prepared for female and male adult patients after lubrication with 5% compound lidocaine cream (Tsinghua Tongfang, China). For pediatric patients, various cuffed and uncuffed SLTs are available. A recent survey by Li *et al.*^[20] revealed that 45.3% (136/300) and 21.3% (64/300) adult patients who underwent cardiovascular surgeries at Fuwai Hospital experienced postoperative sore throat and voice hoarseness, respectively. The reason remains to be further investigated.

2. Double lumen tube intubation

Double lumen tube (DLT) is used in patients undergoing surgical repair of thoracoabdominal aortic aneurysm (TAAA), pulmonary endarterectomy (PEA), video-assisted thoracoscopic cardiac surgeries (VATCS), etc. After placement, the proper position of DLT is routinely confirmed by fiberoptic bronchoscopy (FOB). At the end of procedure, DLT is replaced by SLT before transferring patient to the SICU.

3. Laryngeal mask airway

Laryngeal mask airway (LMA), a supraglottic device, has many advantages over ETT, such as no need for laryngoscopy, easier insertion, fewer hemodynamic and airway complications. The use of LMA in cardiovascular surgical patients has been reported in situations such as temporary airway control during anesthesia induction, difficult endotracheal intubation or face mask ventilation, and accidental intraoperative endotracheal extubation. At Fuwai Hospital, LMA is used in inhalational induction in pediatrics, fast-tracking anesthesia for simple congenital heart diseases repair/endovas-

cular procedures/TAVR, etc. Zhang *et al.* also reported the use of Proseal LMA for airway management in 16 pediatrics undergoing surgical correction of congenital heart diseases complicated with congenital tracheal stenosis at Fuwai Hospital.^[21]

4. Difficult airway

It has been reported that, adult and pediatric patients undergoing cardiac surgery had a significantly higher rate of poor direct laryngoscopic view (Cormack-Lehane Classification Grade 3/4) compared with general surgical patients.^[22] Currently, the prevalence of difficult airway at Fuwai Hospital is unknown. The "Cannot Intubate Cannot Ventilate (CICV)" situation which is a rare occurrence, once happened, could be disastrous for patients with cardiovascular diseases. Difficult airway management should involve anesthesiologists, otorhinolaryngologists, cardiovascular surgeons, perfusionists, intensivists, and professionals in other relevant medical specialties. Difficult Airway Algorithm at Fuwai Hospital is adapted in line with published guidelines, consensus and experts' opinions^[23,24] by considering available institutional resources (e.g., devices, equipment, techniques) and cardiovascular surgical patient characteristics (e.g., vulnerable to hypoxia and hemodynamic instability). In addition to UEScope, other optional tools for airway management in the Anesthesia Department include Macintosh/Miller laryngoscopies of various sizes, FOB, Shikani Optical Stylet (SOS),^[25] etc. (Table S2)

V. Myocardial protection

1. Hypothermia and cardioplegia

The etiology of perioperative myocardial injury is multifactorial, including but not limited to instable hemodynamics, inappropriate protection, inadequate revascularization, myocardial ischemia reperfusion injury (MIRI), etc.^[26] The controversy over the benefits of normothermic vs. hypothermic CPB in cardiac surgical patients remains inconclusive. At Fuwai Hospital, moderately hypothermic CPB (nasopharyngeal temperature at approximately 30°C) is employed in most cardiovascular surgical procedures.^[9] Besides, cold modified St. Thomas crystalloid cardioplegia and 4:1 cold blood cardioplegia (CBC) are used for myocardial protection during aortic cross clamping (ACC) in pediatric or adult patients, respectively. Ice slush is used for topical hypothermia. Warm blood cardioplegia (WBC) is sometimes used before ACC release to wash out myocardial

metabolic products and gaseous microemboli in the coronary circulatory system. Histidine-tryptophan-ke-toglutarate (HTK) cardioplegia Custodiol (Franz Ko-heler Chemie, Germany) is used in some complex and lengthy procedures.^[9]

2. Ischemic preconditioning

Preconditioning and postconditioning have been shown to reduce myocardial damage caused by MIRI. Ji *et al.*^[27] from Fuwai Hospital randomized 40 CABG patients to receive either CBC ($n=20$) or ischemic pre-conditioning (IPC) plus CBC ($n=20$), and the results suggested that IPC combined with CBC significantly decreased postoperative cardiac troponin I (cTnI) re-lease, improved cardiac index (CI), and shortened mechanical ventilation duration(MVD) as compared to CBC alone. However, IPC has not been widely applied in the clinical setting due to concerns of aortic maneu-ver-associated risks and surgical procedure delay.

3. Sevoflurane conditioning

Numerous evidence has indicated that, volatile anesthetic agents (isoflurane, sevoflurane and des-flurane) have the potential to provide organ(*e.g.*, heart, kidney, brain) protection *via* pre- and post-con-ditioning-like mechanisms.^[28] Most CPB machines at Fuwai Hospital are equipped with sevoflurane vapor-izers, enabling sevoflurane administration during CPB for anesthesia maintenance and the employment of sevoflurane preconditioning (SPreC) and sevoflurane post-conditioning (SPostC). Li *et al.* from Fuwai Hospi-tal translated the experimental evidence of SPreC and SPostC into clinical practice. For example, they includ-ed 40 patients scheduled for on-pump CABG and ran-domized them into group SpostC (2% sevoflurane for 15 min upon ACC release) or group Control (no sevo-flurane treatment). It demonstrated that, SpostC sig-nificantly lowered postoperative cTnI, creatine kinase (CK)-MB concentrations, and lactate dehydrogenase (LDH).^[14] In another RCT study evaluating the cardio-protective efficacy of different modalities of SpostC in 75 on-pump CABG patients, they demonstrated that continuous 3.4% SpostC upon ACC release for 15 min was the most potent modality in attenuating myocardi-al injury with respect to myocardial injury biomarkers and ultrastructure.^[13]

4. Remote ischemic conditioning

Remote ischemic conditioning (RIC) refers to that brief, reversible episodes of ischemia with reperfu-sion in one tissue or organ (*e.g.*, limbs) can confer a

global protective phenotype and render remote organs (*e.g.*, heart) resistant to ischemia/reperfusion injury. Meta-analyses by Yao,^[31] Yang^[32] and Zhang^[33] from Fu-wai Hospital confirmed the cardioprotective efficacy of remote ischemic preconditioning (RIPC) in adult and pe-diatric patients undergoing cardiovascular surgeries. Re-cently, Wang and colleagues from Fuwai Hospital inves-tigated whether RIPC combined with remote ischemic postconditioning (RIPostC) could reduce myocardial injury of donor hearts in patients undergoing orthotopic heart transplantation.^[34] One hundred and twenty pa-tients scheduled for heart transplantation were enrolled and randomly assigned into RIPC+RIPostC group ($n=60$) or control group ($n=60$). The findings indicated that, RIPC+RIPostC significantly reduced serum cTnI levels at 6 h after aortic declamping, but there was no signifi-cant difference with respect to in-hospital morbidity and mortality between the two groups.^[34]

5. Other cardioprotective drugs

Other drugs proven to have cardioprotective pro-files at Fuwai Hospital include ulinastatin,^[35] creatine phosphate,^[36,37] cardiomyopeptidin,^[38] adenosine,^[39,40] levosimendan,^[15] and dexmedetomidine.^[41]

VI. Mechanical circulatory support

1. Intra-aortic balloon pump (IABP)

The initial clinical utilization of IABP, ventricular assist device, and extracorporeal membrane oxygen-ation at Fuwai Hospital was in 1982,^[42] 1995,^[43] and 2004,^[44] respectively. IABP is the first-line mechanical support modality for adult patients undergoing car-diovascular surgery. At Fuwai Hospital, indications of preoperative IABP insertion include cardiogenic shock, refractory angina pectoris, heart failure, *etc.* Indica-tions of intraoperative IABP insertion include difficult CPB weaning, severe hemodynamic instability after CPB, *etc.* Indications of postoperative IABP inser-tion include refractory low cardiac output syndrome (LCOS), intractable cardiac arrhythmia, bridge to oth-er mechanical supports (*e.g.*, ECMO), *etc.* Recently, Zhou *et al.* retrospectively analyzed the outcomes of IABP-supported patients undergoing CABG at Fuwai Hospital during 8-year period. Totally, 15,764 pa-tients underwent primary and isolated CABG at Fu-wai Hospital from January 2008 to December 2015. The incidence of IABP implantation in CABG patients was 0.21% (313/15, 764).^[45] The mortality rate of IABP-treated patients was between 14.1% and 16.6%.

[45,46] Advanced age, female, and enlarged left ventricular end diastolic dimension were independent risk factors of mortality in patients after IABP implantation. Proactive IABP application preoperatively or intraoperatively could reduce mortality as compared to rescue IABP implantation postoperatively. The most common complications after IABP therapy were hemorrhage (2.5%-2.7%) and limb ischemia (1.7%-4.8%). Advanced age, diabetic mellitus, and concomitant ECMO support were independent risk factors of IABP-associated complications.^[45,46]

2. Extracorporeal membrane oxygenation (ECMO)

ECMO is a technique capable of providing circulatory and pulmonary support for patients who is refractory to conventional therapy. At Fuwai Hospital, ECMO is indicated mainly as follows: 1) failure to wean from CPB or LCOS even on high dose inotropic agents or IABP support; 2) patients who experience cardiac arrest but is effectively resuscitated and intubated; 3) as bridge-to-transplantation; 4) severe hypoxia ($\text{PaO}_2/\text{FiO}_2 < 60$ when inhaling 100% oxygen).^[47,48] Gao *et al.*^[48] retrospectively reviewed the clinical data of 142 adult patients receiving ECMO therapy from December 2004 to December 2014. ECMO was indicated due to failed CPB weaning in 59 (41.5%) patients, and due to LCOS in 44 (31.0%) patients. In 37 patients, IABP was concomitantly used with ECMO. ECMO was successfully weaned in 99 (69.7%) patients, and 84 (59.2%) patients survived. The most frequent complication during ECMO support was bleeding from catheterization or operative site (45.8%).

In 2019, ECMO was used in 44 adult and 11 pediatric patients at Fuwai Hospital, and the overall survival rate in ECMO-supported patients was 61.8%.^[3] The survival rates on postoperative 30 day of ECMO-treated adults and pediatrics were 63.6% (28/44) and 54.5% (6/11), respectively.

3. Ventricular assist device (VAD)

At Fuwai Hospital, VAD is utilized as 1) bridge-to-transplantation (BTT), 2) bridge-to-recovery (BTR), 3) destination therapy (DT), and 4) bridge to decision (BTD).^[3,49,50] Since 1995, a variety of VADs (*e.g.*, Abiomed BVS5000, MEDOS, AB5000, Novacor) have been utilized at Fuwai Hospital. Luo *et al.*^[50] summarized 12 male patients (aged 39 to 68 years) supported with Abiomed BVS5000 during the period from February 2004 to April 2006 at Fuwai Hospital. BVS5000-VADs were implanted in 11 patients due to

post-CABG LCOS as BTR and in one patient with dilated cardiomyopathy as BTT. The support duration ranged from 3 to 43 days, the successful weaning rate and discharge rate was 75% (9/12) and 67% (8/12), respectively. The most common morbidities during BVS5000 support were neurological complications, bleeding, and infection. As in the 2019 annual report on outcome of cardiovascular surgery by Fuwai Hospital,^[3] CH-VAD, the first-generation magnetic suspension centrifugal blood pump with complete independent intellectual property rights of China, was launched in June 2017 by Professor Shengshou Hu, the president of Fuwai Hospital, and his team of artificial heart development. In January 2018, the team also began the clinical evaluation of EVAHEART-I-VAD. Till December 2019, the surgical team at Fuwai Hospital has completed the implantation of 26 CH-VADs and 12 EVAHEART-I-VADs for 21 patients with dilated cardiomyopathy, 11 patients with ischemic cardiomyopathy, 5 patients with valvular cardiomyopathy, and 1 patients with chemotherapeutic cardiomyopathy. It is inspiring that, the 30-day and 1-year survival rates after implantation are 100% and 94%, respectively.

VII. Pulmonary hypertension management

Pulmonary hypertension (PH), defined as a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg at rest and ≥ 30 mmHg during exercise, is a complex pulmonary vasculature disorder caused by multiple etiologies. Cardiovascular surgical patients with PH are at a significant risk of perioperative morbidity and mortality.^[51,52]

Intravenous administration of inodilator milrinone, vasodilator nitroglycerin and inotrope dobutamine are often used to treat PH at Fuwai Hospital. Inhaled nitric oxide (iNO) produces selective pulmonary vasodilation without reducing systemic arterial pressure in patients with PH. At Fuwai Hospital, iNO (2.5 ppm - 20 ppm) is commonly used in managing PH caused by left heart disease (*e.g.*, mitral valvular diseases, left heart outflow tract obstruction) in adults,^[53,54] and pulmonary arterial hypertension (PAH) in pediatric with congenital heart diseases.^[55-58] Nitrogen dioxide (NO_2) production and methemoglobin (MetHb) concentrations are continuously monitored during iNO therapy.^[59-61]

VIII. Blood conservation

Blood loss and transfusion requirement are important quality indicators of cardiovascular surgery. Generations

of cardiovascular surgeons, anesthesiologists, perfusionists, intensivists, and other health care professionals at Fuwai Hospital have devoted themselves to blood conservation. Based on their pioneer work, a multi-disciplinary patient blood management (PBM) strategy was formally initiated at Fuwai Hospital in 2009. It includes the establishment of a three-level administration model, organization of a multiple-disciplinary PBM team, enactment of blood transfusion management protocols, and adoption of a blood consumption announcement and scoring system.^[62] Since 2009, the average consumption of blood products has decreased significantly against the increase of annual surgical volume at Fuwai Hospital. In 2019, the surgical volume of Fuwai Hospital was 14,808, and the transfusion requirements (incidence/volume) of red blood cell (RBC) and fresh frozen plasma (FFP) in adult cardiovascular surgical patients were 25.8%/1.3 units and 14.4%/1.0 unit, respectively.^[3] The transfusion requirements (incidence/volume) of RBC and FFP in pediatric patients during the same period were 62.0%/1.1 units and 18.9%/0.4 unit, respectively.^[3] PBM in cardiovascular surgery is a "team sport" which involves cardiac and vascular surgeons, anesthesiologists, perfusionist and intensivists. The surgeons at Fuwai Hospital have been dedicated to minimizing surgical trauma and enhancing postoperative recovery *via* minimally invasive surgical approaches. The perfusionists have also applied various techniques and devices to reduce allogenic blood products usage.

Many factors contribute to coagulopathy and bleeding in cardiovascular surgical patients, and a variety of hemostatic agents are optional. Aprotinin was the major antifibrinolytic agent at Fuwai Hospital from 1994 to 2008.^[63,64] Currently, tranexamic acid (TXA) is the most widely used antifibrinolytic agent and the mainstay hemostatic agent. Beside TXA, ulinastatin,^[65] fibrinogen concentrates (FC),^[66,67] prothrombin complex concentrates (PCC), recombinant activated factor VII (rFVIIa),^[68] desmopressin (DDAVP),^[69,70] hemocoagulase Agkistrodon (HCA),^[71] vitamin K (VitK),^[72,73] and topic hemostats (bovine collagen sponge, human fibrin sealant, biodegradable hemostatic paper, biomedical glue) are also available at Fuwai Hospital.

IX. Blood glucose management

Blood glucose (BG) dysregulation is common after cardiovascular surgery, as reported in up to 90% of patients with diabetes and in 60% of patients with-

out diabetes.^[74] Despite it remains debated regarding the optimal glucose target for different subgroups of cardiovascular surgical patients, a strong association between hyperglycemia and poor clinical outcome has been well agreed upon.^[74] At Fuwai Hospital, it is a common practice to maintain perioperative BG level between 120-180 mg/dL.

Liu *et al.*^[75] retrospectively analyzed 549 adult patients undergoing aortic arch replacement with deep hypothermic circulatory arrest (DHCA) and demonstrated that, BG levels elevated after CPB initiation and rose significantly after rewarming, then decreased on postoperative day (POD)-2 and returned to baseline on POD-6. Among the 549 patients, 22.0% had peak intraoperative BG levels above 240 mg/dL, which was associated with increased morbidities. In a RCT study^[76] enrolling 70 adult patients scheduled for elective cardiac surgery at Fuwai Hospital, the effects of starch-based colloid 6% HES and gelatin-based colloid 4% gelatin on BG were compared. The incidences of hyperglycemias of the two groups were 62.8% and 42.9%, respectively, and 4 patients (11.5%) in each group experienced glucose values above 180 mg/dL. A retrospective study^[77] from Fuwai Hospital suggested that the incidence of postoperative hyperglycemia (BG>150 mg/dL) and hypoglycemia (BG<70 mg/dL) in pediatrics undergoing surgical correction for complex congenital heart diseases were 58.5% (258/441) and 13.6% (60/441), respectively.

X. Post-operative analgesia

Cardiovascular surgery induces severe postoperative pain, which could destabilize hemodynamics, impair pulmonary function, increase mortality and morbidity, and prolong ICU and hospital stay. In 1998, Wang *et al.*^[79] conducted a pre- and post-operative questionnaire survey involving 200 patients undergoing cardiac surgery at Fuwai Hospital. The preoperative survey data suggested that only 15.0% (30/200) patients agreed that postoperative analgesia was necessary, and 58.5% (117/200) patients worried that postoperative analgesia might result in adverse effects (*e.g.*, opioid addiction, delayed wound healing). The postoperative survey data showed that 65.5% (131/200) patients deemed postoperative analgesia was necessary, 42.0% (84/200) patients reported that postoperative pain was the most horrible experience during their hospitalization.

Patient-controlled analgesia (PCA) technique was

introduced into China in the early 1990s and has now become the most common analgesic treatment for postoperative patients.^[80] Intravenous PCA (IV-PCA) is the most common postoperative analgesic modality at Fuwai Hospital. For adult patients, a solution of sufentanil 100 µg plus dezocine 30 mg and tropisetron 5mg in 100 mL saline is used with an IV-PCA pump, which delivers 2 mL analgesic solution *per* hour. For pediatric patients younger than 6 months, a solution of sufentanil 1.5 µg/kg plus tropisetron 0.1 mg/kg in 100 mL saline is used with an IV-PCA pump, which delivers 2 mL analgesic solution *per* hour, and a solution of sufentanil 2.5 µg/kg plus tropisetron 0.1 mg/kg and dexmedetomidine 10 µg/kg in 100 mL saline is used for pediatric patients older than 6 months. These are the mainstay solutions used in daily postoperative analgesic practice. The safety and efficacy of other analgesic drugs (*e.g.*, fentanyl, morphine, oxycodone hydrochloride, flurbiprofen axetil, tramadol, dexmedetomidine) and other techniques [*e.g.*, subcutaneous PCA, transcutaneous electric nerve stimulation (TENS)] have been investigated at Fuwai Hospital. For fast-tracking cardiovascular anesthesia, incisional infiltration with ropivacaine at the end of procedures is routine. In the future, different regimes should be established for patients in terms of different age groups, different surgical procedures, and different coexisting disorders in order to maximize analgesic effects, minimize side effects, and make every single patient pain-free.

OUTCOMES

I. Mortality

The impact of anesthesia on cardiovascular surgical outcomes remains controversial. Currently, no nation-level data of cardiovascular anesthesia quality in China is available.^[81] Cardiovascular anesthesia safety and quality metrics have been involved into cardiovascular surgical outcomes. Hospital volume, surgeons' and anesthesiologists' caseload have been associated with cardiovascular surgical outcomes.^[81,82] The annual cardiovascular surgical volume at Fuwai Hospital surpassed 10,000 in 2011 and has increased significantly over the last 10 years. Since 2007, Fuwai Hospital has released reports on surgical outcomes annually to the public. In the 2019 annual surgery outcome report,^[3] the cardiovascular surgical volume of Fuwai Hospital was 14,808, and the 30-day post-operative mortal-

ity rate was 0.4%, which has been below 1.0% for consecutive 11 years (**Figure 3A**). Of patients with congenital heart diseases, coronary artery diseases, valvular heart diseases, and aortic diseases, who underwent surgery, the 30-day post-operative mortality rate at Fuwai Hospital in 2019 were 0.2%(8/4468), 0.2%(8/4247), 0.5%(25/5144), and 1.4%(21/1519), respectively (**Figure 3B**). Over the last 10 years, the fast-track system for emergency surgery has significantly improved, and the 30-day post-operative mortality rate of emergency cardiovascular surgeries at Fuwai Hospital has remained below 3.0%, which was 2.3% (19/852) in 2019 (**Figure 3C**).

II. Morbidities

Cardiac arrhythmias are common complications of cardiovascular surgical patients and could be associated with profound sequelae.^[83] The overall incidence of postoperative cardiac arrhythmias in the SICU at Fuwai Hospital was 47.0%. New-onset atrial fibrillation (NOAF) and premature ventricular contraction (PVC) were reported as the two most frequent postoperative cardiac arrhythmias, with the incidence of 33.0% and 11.0%, respectively.^[84] The incidence of perioperative myocardial infarction (PMI) in adult patients at Fuwai Hospital was 0.7% - 1.7%.

Perioperative stroke is also a severe complication in patients undergoing cardiac surgery. The stroke prevalence of cardiovascular surgical patients at Fuwai Hospital is less than 1.0%.^[64,65] Post-operative delirium(PD) is an acute brain dysfunction following surgery, featuring acute onset and fluctuating occurrence.^[85] The incidence of PD at Fuwai Hospital ranges from 6.3% to 47.7%.^[86-88] Post-operative cognitive dysfunction(POCD) is also a common central nervous system complication in patients after cardiovascular surgeries.^[85] The reported incidence of POCD in patients undergoing cardiovascular surgery at Fuwai Hospital ranges from 39.8% to 55.3% one week after cardiac surgery, and 6.4% to 13.1% 3 months later.^[88]

Seizure, transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain, increases the risk of neuronal injury and neuronal networks alteration. The reported incidence of post-operative seizure at Fuwai Hospital is between 0.7% and 1.1%.^[65] Intraoperative awareness is a dreadful complication, which could result in psychological sequela such as posttraumatic stress disorder(PTSD).^[89] The incidence of confirmed

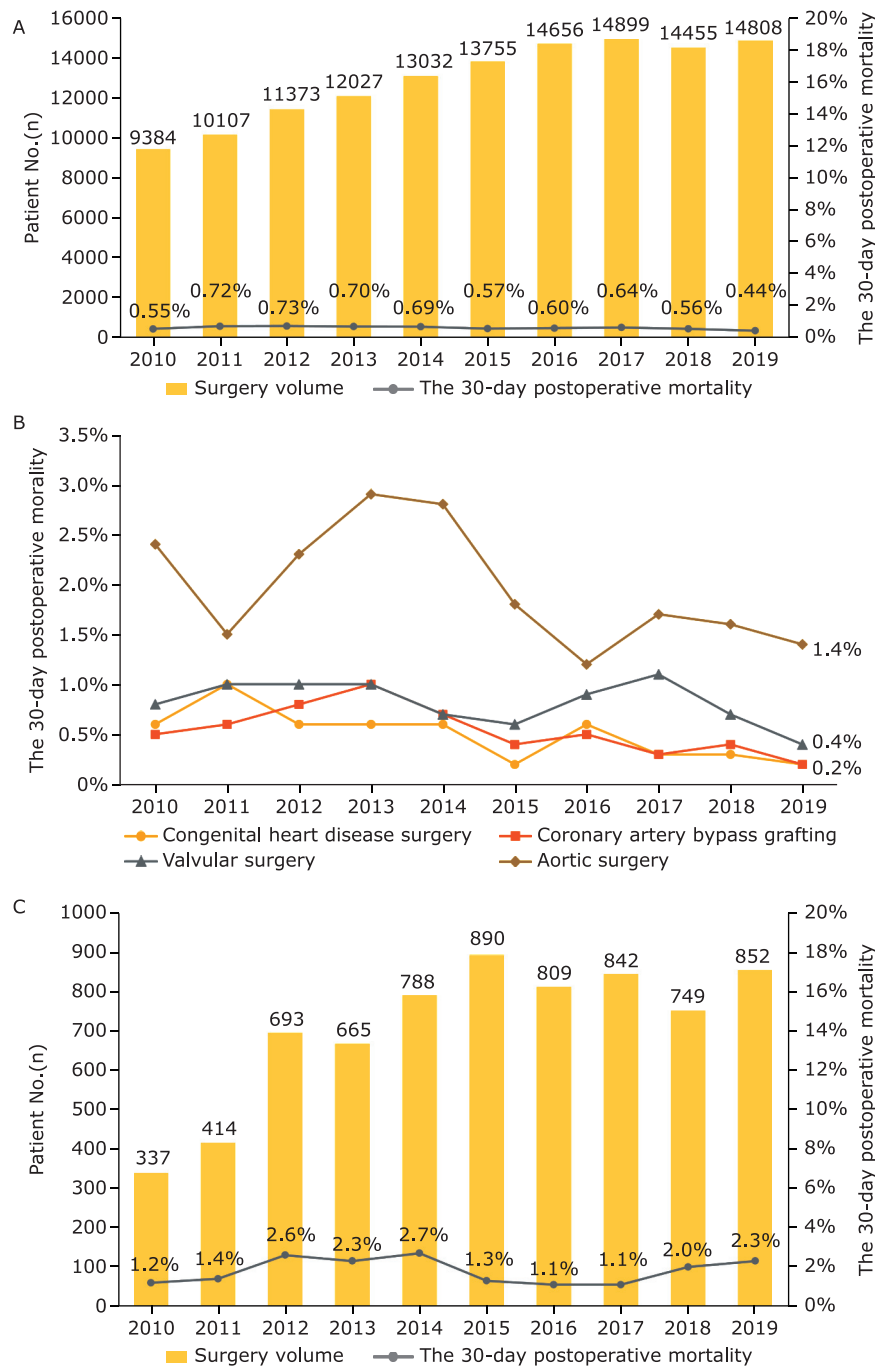


Figure 3. The surgery volume and 30-day postoperative mortality at Fuwai Hospital during period of 2010-2019 (A) Annual surgical volume and mortality in total, (B) of different type of surgeries, and (C) of emergency surgeries.

awareness at Fuwai Hospital was 2.5%-4.5% according to the modified Brice Interview questionnaire.^[90]

For patients undergoing thoracic aorta or thoracoabdominal aorta surgery at Fuwai Hospital, cerebrospinal fluid drainage (CSFD) is performed by anesthesiologists, and intra- and post-operative cerebrospinal fluid (CSF) pressure monitoring in conjunction with other neuroprotective strategies minimize the risk of

neurological sequelae (e.g., paraplegia). Zhou *et al.*^[91] retrospectively analyzed the clinical data of 7,724 patients who underwent open aortic surgery at Fuwai Hospital, found that 64 (0.83%) of these patients suffered from spinal cord injury (SCI). The onset of SCI was immediate in 60.9% (39/64) patients and was delayed in 39.1% (25/64) patients.

Acute kidney injury (AKI), characterized by sudden

kidney function deterioration (e.g., reduced glomerular filtration rate), is a disease spectrum presenting from mild renal dysfunction to dialysis-dependent renal failure. The reported incidence of AKI in cardiovascular surgical patients at Fuwai Hospital varies from 7.5% to 77.6%, with the dialysis dependence incidence between 7.9% and 58.9%.^[92-94]

The spectrum of postoperative pulmonary complications (PPCs) in cardiovascular surgical patients ranges from transient hypoxemia, acute respiratory distress syndrome (ARDS), pulmonary infection, atelectasis, pulmonary edema, etc. For example, the reported incidences of postoperative pulmonary infection and atelectasis at Fuwai Hospital were 5.8% and 1.7%, respectively.^[95,96]

PROSPECTS

To establish the cardiovascular anesthesia quality control institute and cardiovascular anesthesia adverse event reporting system has been planned by national organizations, such as the NSCVA and the CSCVA. A recent survey^[20] indicates that currently, there are still spaces to improve the anesthesia practice in several aspects. Enhanced recovery after surgery (ERAS) programs are developing rapidly in multiple specialties. However, the use of ERAS in cardiac surgery is currently lacking and not well defined.^[97,98] Early postoperative endotracheal extubation and fast-tracking cardiac anesthesia (FTCA) techniques have been utilized for cardiovascular surgical patients at Fuwai Hospital for decades. Recently, surgeons, anesthesiologists, perfusionists, and intensivists at Fuwai Hospital have successfully implemented ERAS program in patients undergoing TAVR, CABG, simple and complex congenital heart diseases correction, TEVAR, EVAR, etc.^[99,100] Optimal analgesia is an integral part of ERAS program. High-dose opioid anesthesia prolongs postoperative mechanical ventilation and the length of stay (LOS) in the ICU. Regional anesthetic techniques represent a promising alternative.

As anesthesiology is one of the most stressful medical disciplines, anesthesia physicians at Fuwai Hospital are exposed to high workload, long work-time, and challenging situations. It is important to reduce physicians' burnout, improve their wellbeing, and safeguard patient safety. How to improve the working schedule and coping strategy is currently under investigation.

Conflict of interests

None.

Supplementary materials

available online at <http://cmsj.cams.cn/EN/10.24920/003924>.

Table S1. The milestones associated with development of the Anesthesia Department, Fuwai Hospital

Table S2. Overview of equipment/device in the Anesthesia Department, Fuwai Hospital

Table S3. Anesthetics and other intraoperative drugs and regimens applied at Fuwai Hospital

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