# Affected organs

#### Cerebral

Brain is the organ most prone to ischemic damage. Cerebral malperfusion is not a rare finding in acute aortic dissection and has been reported to be an important risk factor for in hospital mortality [4].

Cerebral malperfusion is usually due to compression of true lumen by high-pressured false lumen [32]. However, thromboembolism may also plays a significant role [33], and in such cases, thrombectomy may be indicated [34]. As mentioned earlier, axillary artery cannulation at earliest convenience is reported to be useful to ameliorate cerebral malperfusion. However, there are sporadic reports of new or persistent malperfusion with this technique [35]. Persistent malperfusion may be due to complex dissection of carotid artery, and partly due to malposition of the cannula [36, 37], therefore cannulation technique should be as meticulous as possible.

Therapeutically, as noted earlier, asymptomatic cerebral malperfusion leads to prioritizing central repair, while symptomatic cerebral malperfusion should be treated preceding peripheral revascularization, either with percutaneous catheter intervention [28] or carotid bypass [38] or those immediately after the central repair [39].

# Spinal

Postoperative paraplegia may happen even in a chronic phase [40, 41]. Insertion of a spinal catheter is indicated as soon as there are signs or symptoms of spinal cord injury to drain spinal fluid and maximize the effect of elevated spinal cord perfusion pressure [42].

# Cardiac (Coronary)

In patients with acute type A aortic dissection, shock can be caused not only by coronary malperfusion, and cardiac tamponade due to aortic rupture, but also by other pathologies such as left ventricular outflow obstruction [43], infective endocarditis, myocardial infarction, and tuberculosis [44]. Right coronary artery is more frequently involved from the left [32]. Concerning the diagnosis, if coronary malperfusion is strongly suggested, coronary angiogram may be indicated with subsequent coronary stenting with low balloon pressure for left coronary malperfusion; right coronary malperfusion may be treated with surgery or coronary stenting if malperfusion is diagnosed in catheterization laboratory [45]. Apart from routine imaging modalities, ST change in preoperative electrocardiogram has diagnostic value of not only coronary malperfusion, but also other abnormalities such as aortic regurgitation and cardiac tamponade [46]. Unless the patient is in severe shock status due to coronary malperfusion, although basic principle of coronary reconstruction is surgical concomitant with aortic repair, either with coronary artery bypass grafting or button reconstruction with root repair, immediate revascularization with catheter-based intervention prior to definitive aortic repair is associated with favorable outcome [45], therefore tailor-made judgment in individual case is appropriate. Once salvaging myocardium was failed, circulatory support, such as left ventricular assisting device, is inevitable with poor clinical outcome [47]. Cardioplegia is rarely a topic of debate in this regard presumably because the majority of the cases are with good ventricular function preoperatively, and our preference is retrograde cardioplegia at first dose, and then antegrade cardioplegia through the prosthesis after completing proximal anastomosis therefore no cardioplegia cannula can cause iatrogenic dissection/damage around the coronary orifice [48].

Cardiac plus valvular due to commissural detachment

There is a special pathology which causes malperfusion of coronary and left ventricular outflow tract simultaneously, in which aortic dissection occurs in sinus of Valsalva, and aortic intima involving commissure(s) results in coronary malperfusion, left ventricular outflow obstruction and/or aortic regurgitation [49]. Because of the rarity and complexity of its pathophysiology, reaching accurate diagnosis can be difficult, at least time consuming, thus may lead to delay in definitive treatment.

# Mesenteric

Among all malignant phenomena associated with malperfusion syndrome, visceral malperfusion is the most lethal, associated with poor prognosis. Mortality of those with mesenteric malperfusion triples was compared with those without malperfusion [50]. Prognosis becomes even poorer unless malperfusion is corrected and/or necrosed gut is excised [32]. In fact, medical management is noneffective, associated with 95 % hospital mortality, whereas endovascular treatment including fenestration, branch stenting in the same hospitalization halves the mortality [50]. In advanced visceral malperfusion, initial ascending aortic repair and post-repair laparotomy have high mortality rates. Theoretically, this mortality could be reducible if malperfusion is first treated. However, operative delay is also associated with significant mortality due to aortic rupture [28]. Therefore, currently prevailing consensus should be that, in the absence of ongoing or exacerbating severe visceral ischemia with bowel necrosis, central aortic repair should be prioritized. If the degree of visceral damage is



uncertain, laparotomy should come first to determine which procedure, central repair, visceral revascularization or gut resection should be prioritized. At present, clinical dilemma exists as how to prioritize central or peripheral repair, or even triage the patient. Although currently the number of patients treated with hybrid strategy of surgical and endovascular is limited, hybrid operating room may help surgeons' liberal use of several treatment options in liberal timing [9, 50]. Laparoscopy with experienced hands can be also useful in the diagnosis of visceral malperfusion and even in the treatment if affected lesion(s) are limited [51, 52].

# Renal

Impact of renal malperfusion on mortality and morbidity is still unknown. Although renal malperfusion is frequently associated with oliguria and/or hematuria, it often is overlooked clinically because of the lack of clear symptom(s). Emergency intervention is rarely indicated; therefore, usually central repair is prioritized. Surgeons need to differentiate the impact of renal malperfusion and perioperative acute kidney injury. In many papers, impact of renal malperfusion is not paid attention [32, 53] or reported not to be a risk factor for mortality [54], or reported to be a risk factor in univariate analysis, not in multivariate analysis [4]. However, acute kidney injury is reported to be the independent risk factor for mortality and morbidly in many articles [4, 53, 55]. These phenomena may indicate that renal malperfusion is frequently associated with other types of malperfusion such as limb or mesenteric, and/or patients with malperfusion syndrome require multiple investigations with contrast medium, which exacerbates renal function significantly.

# Limb

Although pulse deficit (most commonly lower limb) is reported to be an independent risk factor for death in various studies [53, 56], it usually does not affect survival outcome unless accompanied by malperfusion elsewhere [32]. Evidences of postoperative acute renal failure associated with limb malperfusion, presumably related to reperfusion injury or contrast investigation, are contradictory, and under debate [57, 58]. Standard surgical therapy with restitution of true lumen flow successfully resolves limb malperfusion in most cases, but some requires additional (preceding or concomitant) surgical bypass [59] or endovascular procedures [32] with or without thrombectomy. However, if ischemic damage appears severe, and time to surgical revascularization appears detrimental, external shunt from brachial arteries should be applied [60].

# Should we perform surgery for all?

Severe neurological damage or coma

Although there is a sporadic report of good clinical outcome, patients with severe neurological deficits or coma have poor postoperative outcome [32]. There is so far no consensus as to whether or not definitive aortic repair should be performed promptly [61], or should be delayed until neurological status is stabilized [28] and as to which degree of cerebral damage is likely/unlikely to recover postoperatively. There has been a debate concerning the surgical indication of the central repair for the patients with stroke of significant size, because of the concern of its hemorrhagic conversion [1, 32]. However, recently several authors have reported favorable outcomes of early surgical repair for the patients with severe neurologically deficits, even with coma. Estrera et al. [61] reported for patients with preoperative stroke and type A aortic dissection, neurological status completely recovered in 14 %, and worsened in 0 %. Tsukube et al. [62] reported in patients with coma, hospital mortality is 14 % after early surgery with full recovery of consciousness achieved in 86 %.

Time of surgery and postoperative neurological status scale have been reported to correlate with lack of neurological improvement [63]. Again, there has been no consensus as to the threshold of the time between the onset and therapy; there are sporadic reports of favorable outcome approximately 5 [62] to 10 [61] h. Decompressive craniectomy may help recovering postoperative ischemic damage due to malperfusion syndrome, especially in young patients [64, 65].

# Age

The incidence of acute type A aortic dissection increases with age [66], and age is the independent predictor of worse operative mortality and morbidity and reduced longer term survival even when data are analyzed in mixture of those with and without malperfusion [32]. In fact, in one study, the risk of operative mortality for acute type A aortic dissection is reported as high as 45 % for patients 80–84 years old, and 50 % for those of age 85 and older [67]. There are other studies which reported better clinical outcome with surgery for the elderly [68, 69]. Evidences are contradicting.

Surgeons need to know the individual patients' capacity to reverse the bad prognosis of the disease to answer the question whether surgical therapy should be proposed to those patients. Symptoms of malperfusion such as stroke, coma, visceral ischemia were associated with extremely high mortality rate, and it is particularly true if those symptoms are associated with octogenarians, and it appears

that they should be considered for denial of surgical intervention [70].

# Delayed presentation (>48 h after symptom onset)

Untreated mortality of acute type A aortic dissection has been reported to be  $\sim 1-2~\%$  h after symptom onset, and 24 h mortality was higher than 35 % and more than half of the patients die within 48 h [32]. However, patients with acute type A aortic dissection who are referred from outside hospital or whose conditions are diagnosed several days after the symptom onset have survived the initial perilous period. In such cases, aggressive anti-impulse therapy, detailed evaluation of the severity of the central and peripheral disease, and optimization of the clinical condition and peripheral repair for malperfusion prior to central repair are justifiable, with favorable clinical outcome in significant size of the patients [69].

# Previous cardiac surgery

Adhesions from previous cardiac surgery have been proposed to prevent rupture and tamponade, and thus decrease in the risk of hemodynamic instability. In addition, there was a significant higher mortality in patients with previous cardiac surgery [71]. Although that hypothesis is not yet verified in a large size patient cohort, in cases that patients with previous cardiac surgery exhibit malperfusion, optimization of operative strategy with possible preceding peripheral repair should be seriously considered because of smaller likelihood of aortic rupture.

# Presence of pericardial effusion with hemodynamic stability

In operating acute type A aortic dissection with hemopericardium, surgeons often discover that there is no ongoing active bleeding. Meanwhile, sudden rupture occurs intraoperatively, indicating there is a certain group of patients with cardiac tamponade who endure operative delay and who may not. Although it is doubtless that patients with acute type A aortic dissection are exposed to high risk of aortic rupture, in one study, aortic rupture at the time of surgery is not associated with the increase of the hospital mortality or permanent neurological complication significantly [72]. This suggests that in the treatment of acute type A aortic dissection with malperfusion and hemodynamically stable hemopericardium, preceding peripheral repair with or without pericardiotomy can be a treatment of choice, especially with a hybrid operating room where surgeons can perform subsequent or simultaneous central repair once real aortic rupture occurred.

#### Conclusion

Malperfusion syndrome associated with acute type A aortic dissection is associated with poor clinical outcome, especially with cerebral and visceral malperfusion. Accurate and timely diagnosis with imaging and monitoring modalities, not only preoperatively but also intra and postoperatively, and tailor-made treatment (i.e., delayed central repair with prior peripheral revascularization or central repair with subsequent peripheral repair) with "liberal mind and liberal use of medical and surgical resource" is mandatory for decreasing the mortality.

Conflict of interest Takeshi Shimamoto and Tatsuhiko Komiya both have no conflict of interest.

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# ADVANTAGES OF THE CONTINUOUS TELESCOPIC INVERSION TECHNIQUE DO NOT OVERCOME THE DISADVANTAGES OF THE "TURN-UP" TECHNIQUE OF AORTIC ANASTOMOSIS To the Editor:

Rylski and associates<sup>1</sup> should be congratulated for the favorable outcomes of the continuous telescopic anastomosis technique applied for a diseased aorta and Dacron prosthesis. They mentioned that their technique is superior to our "turn-up" anastomosis method (2-layer anastomosis involving 6 to 8 pairs of firstline everting U stay sutures followed by second-line continuous over-andover sutures), because they believe their method requires less time and does not have a ridge projecting into the bloodstream. We wish to correct their misunderstanding, explain what defines good anastomosis to the readers of the Journal, and present the advantages of the turn-up method.

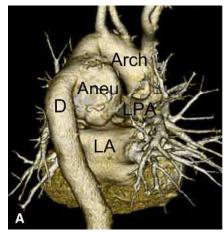
In the technique reported by Rylski and colleagues, external felt is placed separately from the sutures, which takes additional time. However, in the turn-up method, external felt for strengthening the distal aorta is simultaneously placed with 6 to 8 U stay sutures, which are placed for everting 3 to 5 mm of prosthetic edge in preparation for the second layer of anastomosis. In this sense, both methods require 2 layers for complete anastomosis. However, we do not recommend reducing the number of first-line U stay sutures to save time; at least 6 pairs are necessary for effective eversion.

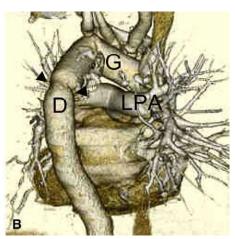
With regard to technical difficulty, in the method described by Rylski and associates, the suture goes out-in the aorta, then out-in and in-out the prosthesis, which indicates that the surgeon has to frequently change the direction of the needle. This complexity may prevent others from using this technique for the distal aorta, particularly near the bronchial artery, because surgeons find it difficult to place the sutures at the nadir of the deep arterial valley. In fact, they predominantly use this technique for the proximal aorta. Meanwhile, the turnup method involves only forehand suturing and can be used regardless of the position of the anastomosis, that

is, proximal, distal, or very distal (Figure 1). Moreover, because the first-line sutures are carefully placed separately, adventitia is not missed even with very diseased aortas, and it is much easier to place second-line sutures by retracting the prosthesis and grasping the everted portion.

With regard to hemostatic power, the technique of Rylski and associates basically involves 1-layer continuous sutures, with the prosthesis placed inside the aorta; thus, hemostasis is achieved by a single suture line. In the turn-up method, second-line continuous over-and-over sutures are placed along the everted portion, and hemostasis is achieved by a suture band 3 to 5 mm in circumference, which seems more stable. Moreover, even if anastomotic bleeding occurs, additional sutures can easily be placed along the everted prosthesis and aortic wall.

From January 2003 to October 2010, our turn-up technique was used for 440 aortic aneurysm cases and 170 Stanford A aortic dissection cases. Although needle hole bleeding from the fragile dissected aorta occurred occasionally, there has been no re-exploration for bleeding from the anastomosis and no postoperative false aneurysms occurred due to this technique. Further, no ridge because





**FIGURE 1.** A, Preoperative 3-dimensional computed tomographic image in the dorsal view of a patient with a huge distal arch aneurysm; the diameter of the aneurysm was normalized behind the bifurcation of the pulmonary artery. B, Postoperative image of the same patient as in A. The arch and proximal descending aorta were completely replaced with a prosthesis (*arrowhead*) placed through a median sternotomy without any additional incision. *Arch*, Aortic arch; *Aneu*, aneurysm; *LPA*, left pulmonary artery; *D*, Descending aorta; *LA*, Left atrium. B, *G*, prosthetic graft.

of the everted prosthesis or postoperative hemostasis associated with anastomotic distortion was noted. Thus, the effectiveness of the turn-up method was confirmed with a significantly sized patient cohort and suitable follow-up period.

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# **Reply to the Editor:**

We read with interest the letter of Shimamato and Komiya comparing our novel technique for aortic anastomosis using telescopic graft inversion<sup>1</sup> with the "turn-up" method.<sup>2</sup> We appreciate all thoughtful comments and would like to address some of the important points involved.

First of all, Shimamato and Komiya discussed the time needed for the 2 suture techniques. Both anastomotic techniques are time-consuming. We reported that our method may take about 40% longer than the simple "over-and-over" technique. Both "turn-up" and graft telescopic inversion methods involve 2 layers of sutures for complete anastomosis. However, the easy mattress suture of felt strip in our technique extended the time for anastomosis only slightly. Additionally, there was no need for hemostatic stitches after completing the anastomosis, which might save time. Our method thus reduced the total time for the procedure significantly, mainly because we needed less time

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to stop the bleeding. We are convinced that the addition of the technique of Shimamato and Komiya in selected cases can save overall time and morbidity as well.

In describing our method, we concluded that there is no ridge in the bloodstream in comparison with the "turn-up" method. Inverted Dacron aortic anastomosis results in 1 layer of intraluminal Dacron at the anastomosis level, whereas the "turn-up" technique requires 2 intraluminal layers, which may result in a ridge projecting into the bloodstream. We believe that an anastomotic stenosis or any intraluminal edge can be unfavorable and elicit embolic events. With our method, we try to prevent anastomotic stenosis by completing the anastomosis first, then opening the crossclamp, and carefully tightening and knotting the suture for the external felt with full pressure filling to prevent suspected tourniquet syndrome on the anastomotic side.

We are convinced that both techniques are appropriate for aortic replacement, especially when the arterial wall is highly fragile, as in aortic dissection or in patients with Marfan syndrome. Please allow us to recommend our technique as a worthwhile supplement to the surgical armamentarium that can be used in cases such as those mentioned above.

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# IMMORTAL PERSON-TIME BIAS IN OBSERVATIONAL STUDIES IN CARDIAC SURGERY To the Editor:

We read with great interest the article by Kim and associates<sup>1</sup> in a recent issue of the *Journal of Thoracic and Cardiovascular Surgery*. We find this topic area engaging and relevant to clinical practice, especially in light of expanding indications of dual antiplatelet therapy and recent advances in perioperative management lending to improved acute operative mortality.<sup>2</sup> However, we have important concerns regarding the methodology and statistical analyses undertaken.

The investigators compared the treatment strategies of aspirin plus clopidogrel with aspirin alone in patients undergoing isolated coronary artery bypass grafting (CABG). Dual therapy was associated with a 50% risk reduction (odds ratio [OR], 0.50; 95% confidence interval [CI], 0.25-0.99) in in-hospital mortality, a 30% risk reduction (OR, 0.70; 95% CI, 0.51–0.97) in bleeding events, and no effect on ischemic/thrombotic events (OR, 0.99; 95% CI, 0.59-1.64). These robust, and seemingly contradictory, findings may be influenced by important biases.

First, the exposure measurement was based on the addition of clopidogrel in days 1 and 2 postoperatively, with primary outcome assessment beginning immediately after the operation. Patients must thus survive (ie, are "immortal") those days into the postoperative period to be defined as exposed to the clopidogrel therapy, whereas patients experiencing an adverse event previously were thus necessarily included in the unexposed group (aspirin alone). Such a classification of exposure to clopidogrel leads to immortal time bias.3 The magnitude of this bias is directly related to the proportion of length of stay (not provided in text) that is immortal, with shorter length of stays resulting in higher bias, and the number