Excessively high systemic blood pressure in the early phase of reperfusion exacerbates early-onset paraplegia in rabbit aortic surgery

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Objective: We have demonstrated that therapeutic augmentation of systemic blood pressure during spinal cord ischemia plays an important role in minimizing spinal cord injury in both experimental and clinical aortic surgery. However, there remain concerns that excessively high blood pressure during spinal cord reperfusion may aggravate the reperfusion injury. The purpose of this study is to investigate the effect of high blood pressure during spinal cord reperfusion on postoperative neurologic outcomes after aortic surgery in rabbits.

Methods: Experiments were performed using a rabbit spinal cord ischemia-reperfusion model in 2 randomly divided groups: (1) In the HR group, the mean blood pressure was maintained at a high level (121 ± 1.3 mm Hg) during reperfusion with intravenously administered phenylephrine; and (2) in the CR group, the mean blood pressure was not medically controlled (75 ± 9.1 mm Hg) during reperfusion. Neurologic and histologic assessments and evaluation of early reperfusion injury were performed.

Results: In the HR group, slow and incomplete recovery of transcranial motor-evoked potentials ($P = .02$) and low neurologic scores ($P < .005$) were observed during spinal cord reperfusion compared with the CR group. At 48 hours of reperfusion, there were significantly fewer viable neuron cells, more apoptosis, and more perivascular edema with gray matter vacuolation in the HR group ($P < .001$ for each). At 3 hours, myeloperoxidase activity ($P = .0021$), vascular permeability ($P = .0012$), and superoxide generation ($P < .0001$) were significantly increased in the HR group.

Conclusion: Excessively high blood pressure in the early phase of spinal cord reperfusion increased reperfusion injury in the spinal cord, leading to exacerbation of early-onset paraplegia. Avoidance of spinal cord reperfusion with high blood pressure may be one management strategy in thoracoabdominal aortic surgery. (J Thorac Cardiovasc Surg 2010;140:400-7)

Neurologic complications such as paraplegia or paraparesis are still major concerns associated with thoracoabdominal aortic repairs. The incidence of neurologic complications has gradually declined with advances in surgical techniques and several managements, including preoperative identification of the Adamkiewicz artery, mild or deep hypothermia, distal aortic perfusion, segmental aortic clamping, reconstruction of the intercostal or lumbar arteries, cerebrospinal fluid drainage, monitoring of motor-evoked potentials, and pharmacologic agents. However, definite strategies to prevent the intractable complications with high mortality and morbidity cannot be established.

Spinal cord ischemia (SCI) is of primary importance for the development of paraplegia or paraparesis after aortic surgery. It is well known that temporary interruption of blood flow to the spinal cord during an operative procedure such as aortic crossclamping induces irreversible neuron damage in the spinal cord. However, the blood supply to the spinal cord depends on a highly variable collateral system from the systemic circulation.[1] We recently demonstrated that augmentation of systemic blood pressure (BP) during SCI protects the spinal cord and prevents paraplegia after aortic surgery in an experimental model.[2]

It is well known that spinal cord motor neurons are sensitive and vulnerable to any degree of ischemic insult. Early spinal cord reperfusion (SCR) with sufficient blood flow is important to reduce ischemic injury, but the SCR itself may cause spinal cord cell damage, known as "reperfusion injury." Some investigators have suggested that controlled blood perfusion after ischemia may reduce reperfusion injury in various other organs.[3-5] Although Shi and colleagues[6] demonstrated that controlled low-pressure perfusion at the beginning of reperfusion attenuates neurologic injury after SCI, the impact of BP augmentation during SCR and SCI on the spinal cord in aortic surgery still remains controversial.

Abbreviations and Acronyms
BP = blood pressure
MPO = myeloperoxidase
MTS = modified Tarlov scale
OD = optical density
SCI = spinal cord ischemia
SCR = spinal cord reperfusion
tc-MEP = transcranial
motor-evoked potential
TUNEL = terminal deoxynucleotidyl
transferase-mediated deoxyuridine
triphosphate nick-end labeling

The present study aims to elucidate the effect of high BP during SCR on reperfusion injury in aortic surgery. To focus on the SCR injury (not the SCI injury), we used a rabbit spinal cord ischemia-reperfusion model with a high BP during the SCI for a minimal ischemic injury, based on our recent study.[2]

MATERIALS AND METHODS
Animals
Thirty-six Japanese white rabbits weighing 2.5 to 3.0 kg were obtained from Kitayama Labes Co (Nagano, Japan). The handling of laboratory animals and their use in experiments conformed to the *Guidelines for Animal Experiment at Kobe University Graduate School of Medicine* (permission number: P090309) and the *Guide for the Care and Use of Laboratory Animals* (www.nap.edu/catalog/5140.html).

Surgical Procedure
Experiments were performed using a rabbit spinal cord ischemia-reperfusion model, which we previously described.[7] To establish the SCI, the catheter balloon (Swan–Ganz thermodilution catheter, 93-132-5F; Baxter Health Corporation, Santa Ana, Calif) was fully inflated 0.5 to 1.5 cm distal to the left renal artery for 15 minutes. According to the results of our previous study,[2] the mean BP during the SCI was medically kept at approximately 120 mm Hg for a minimal ischemic injury. After 15 minutes of SCI, the catheter balloon was deflated, and the SCR was performed with an indicated BP that was medically controlled for 15 minutes in its early phase, followed by the natural recovery with no medication until each end point. During the operation, the body temperature was monitored with a rectal thermostat and maintained at 37°C to 38°C using a heating pad.

Experimental Groups
Animals were randomly divided into 2 groups according to the BP level during SCR: 1) the high BP group (HR group), for which the mean BP was maintained at approximately 120 mm Hg by intravenously administered phenylephrine (Neo-Synesin Kowa Injection; Kowa Co, Tokyo, Japan); and 2) the control BP group (CR group), for which the BP was not medically controlled and the mean BP recorded was approximately 80 mm Hg. The mean body weight was not significantly different in both groups.

Neurologic Assessment
Serial assessments of motor function of the hind limbs in all animals were performed at 3, 24, and 48 hours of reperfusion using the modified Tarlov scale (MTS; 0 = no movement, 1 = slight movement, 2 = sits

with assistance, 3 = sits alone, 4 = weak hop, 5 = normal hop), as described previously.[7] Animals with an MTS score of 4 or more were considered to be nonparaplegic, whereas those with an MTS score of 3 or less were considered to be paraplegic in this study.

Measurement of Transcranial Motor-Evoked Potentials
Transcranial motor-evoked potentials (tc-MEPs) were recorded during 15 minutes of ischemia and a subsequent 30 minutes of reperfusion, and the recovery ratio of tc-MEP amplitude was measured and analyzed according to our previous report.[2] The baseline of tc-MEPs was defined as an average of 3 consecutive amplitudes recorded before aortic occlusion, and the reappearance was defined as devoid of flat waves in 3 consecutive responses: recovery ratio of tc-MEPs amplitude = (amplitude anterior tibial muscles baseline anterior tibial muscles) × (baseline anterior radial muscles amplitude anterior radial muscles) × 100 (%).

Evaluation of Pathologic Outcome
The spinal cord sections between L3 and L4 were harvested at 3, 24, and 48 hours of reperfusion and stained with hematoxylin-eosin for histopathologic observation, such as motor neuronal viability,[2] perivascular edema, and gray matter vacuolation. To detect DNA fragmentation in cell nuclei, terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL) staining was performed.[2] Morphometric analyses of spinal cord sections were performed using ImageJ version 1.41 software (National Institutes of Health, Bethesda, Md). Viable neuron cells and TUNEL-positive neurons were counted, and the degree of perivascular edema and gray matter vacuolation were judged by 2 blinded investigators using the following scoring system (0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = severe).

Western Blot Analysis
Immunoblotting assay was performed according to our previous study.[2] The primary antibody used was mouse anti-rabbit caspase 3 antibody (Millipore Corp, Billerica, Mass), and the secondary antibody used was goat anti-mouse immunoglobulin antibody. The signals were quantified by an image analyzer (LAS-3000; FUJI-FILM Corp, Tokyo, Japan). Blots were subsequently probed for β-actin (Bio Vision Research Products, Mountain View, Calif) as an internal control for equivalent protein loading. The optical density (OD) of each band was measured on the same membrane.

Vascular Permeability Assay
Vascular permeability in the spinal cord at 3 hours of reperfusion was assessed by Evan's blue (Sigma-Aldrich, St Louis, Mo) assay, as previously described with some modification.[8,9] After 15 minutes of reperfusion, Evan's blue (50 mg/kg) was injected into the animals intravenously and they were sacrificed at 3 hours. The spinal cord samples were quantified after formamide extraction (55°C for 2 hours) by measuring absorbance at 595 nm. Data were expressed as the OD per gram of wet tissues.

Myeloperoxidase Activity
Myeloperoxidase (MPO) activity in spinal cords at 3 hours of reperfusion was assessed as previously described,[8,10] with some modification. MPO values were expressed as the change in absorbance at 450 nm/min/g of wet tissue.

Superoxide Generation
Superoxide levels during early reperfusion were evaluated on tissue cryosections of the spinal cord between L3 and L4 at 3 hours of reperfusion as previously described.[2] Dihydroethidium (Invitrogen, Carlsbad, Calif) was used as an oxidative fluorescent dye. Semiquantitative analyses of the superoxide generation were performed using ImageJ software. The average fluorescence intensity was expressed as a fluorescence unit per field.

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Statistical Analysis

Database management and statistical analysis were performed with Statview version 5.0 (SAS Institute Inc, Cary, NC). All values are expressed as means ± standard error of the mean. Comparisons between the 2 groups were performed with an unpaired Student t test.

## RESULTS

Intraoperative Blood Pressure Status

In the present experiments, all animals survived until each end point. The intraoperative BP is shown in Figure 1. There were no statistical differences in the mean BP before and during SCI between the HR and CR groups (before, 81.5 ± 6.6 mm Hg vs 82.3 ± 3.6 mm Hg; during 122.4 ± 1.6 mm Hg vs 122.5 ± 2.8 mm Hg). The mean BP in the early phase of SCR was adjusted at 121 ± 1.3 mm Hg in the HR group, whereas it was 75 ± 9.1 mm Hg naturally in the CR group, with a significant difference according to their definition ($P < .0001$).

Transcranial Motor-Evoked Potential Recovery

The tc-MEPs disappeared immediately after aortic occlusion and reappeared after balloon deflation. The tc-MEP recovery time was 17.3 ± 4.2 minutes in the HR group and 10.0 ± 3.1 minutes in the CR group. There was a tendency for a longer recovery time in the HR group than in the CR group, although statistical significance was not reached (Figure 2, A). The recovery ratio of tc-MEP amplitude at 30 minutes of reperfusion in the HR group was significantly lower than in the CR group ($P = .008$; Figure 2, B).

Neurologic Outcomes

The MTS scores at 3, 24, and 48 hours of reperfusion are shown in Figure 2, C. In the HR group, paraplegia was observed in 44% of rabbits at 3 hours, 83% of rabbits at 24 hours, and 100% of rabbits at 48 hours of reperfusion.
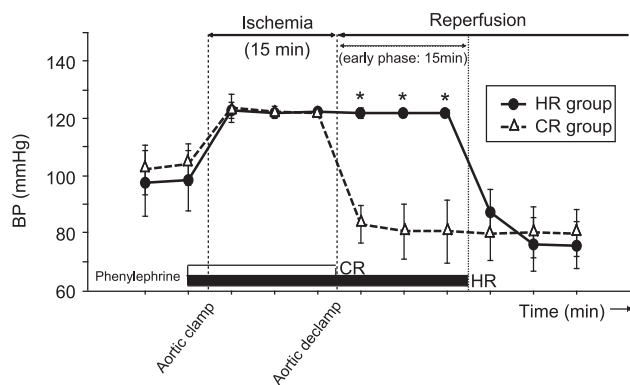
FIGURE 1. Systemic BP during surgery. There were no significant differences in BP during ischemia between the HR and CR groups. In the early phase of reperfusion, BP in the HR group was significantly higher than in the CR group. *$P < .05$. *BP,* Blood pressure; *HR,* high BP group; *CR,* control BP group.

The neurologic score deteriorated with time and were significantly different between the HR and CR groups (3 hours, $P = .0005$; 24 hours, $P = .0032$; 48 hours, $P < .0001$).

Histologic Assessment

At 3 and 48 hours of reperfusion, the number of viable neuron cells in the HR group was significantly less than in the CR group ($P = .0400$ and $P = .0005$, respectively, Figure 3, A, B), and the degree of perivascular edema and gray matter vacuolation in the HR group was significantly larger than in the CR group (edema, $P = .0100$ and $P < .0001$, respectively, Figure 3, A, C; vacuoles, $P = .0030$ and $P < .0001$, respectively, Figure 3, A, D). There were distinct differences between the 2 groups at 48 hours compared with 3 hours of reperfusion.

Spinal Cord Apoptosis

To detect apoptosis in the spinal cord after the SCR, we performed TUNEL staining and Western blot analysis of caspase 3, which is one of the major effectors of neuronal apoptosis.[11] At 48 hours of reperfusion, the number of TUNEL-positive neuron cells in the HR group was significantly more than in the CR group ($P < .0001$; Figure 4, A, B). Compared with the CR group, the protein expression of caspase 3 was significantly up-regulated in the HR group ($P = .0002$l; Figure 4, C, D).

Early Reperfusion Injury

The early response of reperfusion injury is generally initiated by increased fluid filtration, calcium influx, and neutrophil accumulation into tissues.[12] We evaluated the level of vascular permeability in the spinal cord by Evan's blue assay and the extent of neutrophil infiltration by MPO assay. At 3 hours of reperfusion, both Evan's blue level and MPO activity in the spinal cord tissues were significantly increased in the HR group compared with the CR group (Evan's blue, 1.97 ± 0.19 OD/g wet tissue vs 0.66 ± 0.12 OD/g wet tissue, $P = .0012$; MPO activity, 0.15 ± 0.26 ΔAbs/min/g wet tissue vs 0.008 ± 0.006 ΔAbs/min/g wet tissue, $P = .0021$; Figure 5, A, B). To further evaluate the severity of reperfusion injury, we next semiquantified levels of superoxide in the spinal cord by in situ oxidative fluorescent staining. At 3 hours of reperfusion, the intensity of red oxidative fluorescence in the HR group was significantly higher than in the CR group ($P < .0001$; Figure 5, C, D).

DISCUSSION

Although it is not surprising that early reperfusion is important to reduce reperfusion injury, reperfusion itself could bring irreversible cell damage beyond that caused by the preceding ischemia alone. All organ tissues are susceptible to reperfusion injury, but this susceptibility varies among tissues. Given the delicate nature of arterial supply to the anterior spinal cord, it is well known that motor neuron cells of
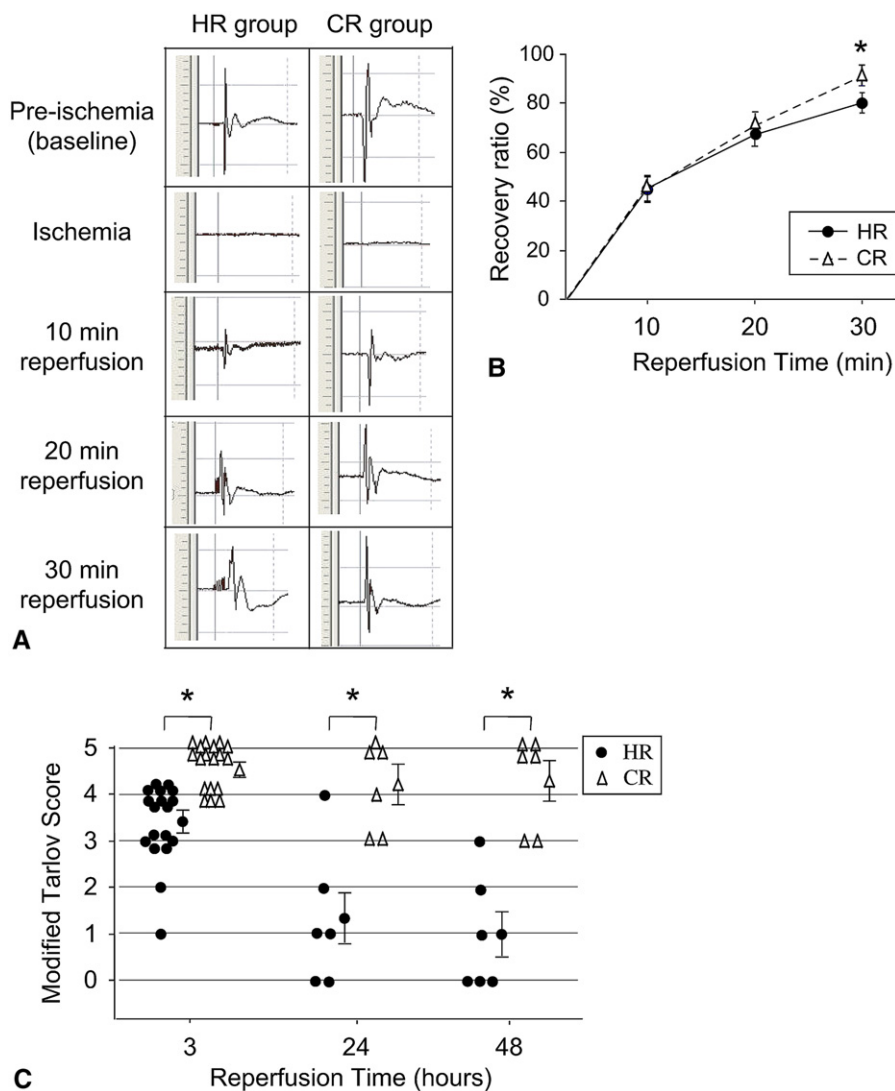
FIGURE 2. Intraoperative and postoperative neurologic assessment. A, Representative tc-MEP complex. B, Recovery ratio of tc-MEP amplitude at 10, 20, and 30 minutes of reperfusion. n = 18 in each group. C, Modified Tarlov score at 3, 24, and 48 hours of reperfusion. n = 18 at 3 hours and n = 6 at 24 and 48 hours of reperfusion in each group. All data are expressed as means ± standard error of the mean (SEM). *$P < .05$. *HR,* High BP group; *CR,* control BP group.

the spinal cord are sensitive and vulnerable to any degree of ischemic insult. In the field of aortic surgery, major intraoperative causes of spinal cord injury are the occurrence of one or more of the following events: (1) the duration and degree of ischemia, (2) the failure to reestablish blood flow to the spinal cord by surgical repair, and (3) the degree of postischemic reperfusion injury.[13] By focusing on the intraoperative management during SCI, we demonstrated that systemic BP augmentation during SCI protected the spinal cord and prevented postoperative paraplegia after aortic surgery in rabbits.[2]

The current study represents a consistent approach to the improvement of strategies to attenuate spinal cord injury in aortic surgery by focusing on the intraoperative management during SCR. Our first concern in the current study was

whether subsequent BP augmentation during SCR, as high as during SCI, could have a beneficial effect on the spinal cord in aortic surgery because blood supply to the spinal cord is partially maintained through the collateral circulation. In contrast, some investigators have shown that controlled reperfusion with a low flow or pressure,[4-6] or gradual reinstitution of reperfusion flow,[3] limited reperfusion injury in their setting of experimental ischemia-reperfusion. However, the impact of controlled reperfusion with high pressure on the spinal cord, which has a complex blood supply system during thoracoabdominal aortic surgery, remains unclear. Our recent study[2] showed that rabbits with a BP of 120 mm Hg during the 15-minute SCI had a reduced ischemic insult, resulting in less neuronal damage. By using this model with the same ischemic conditions, we
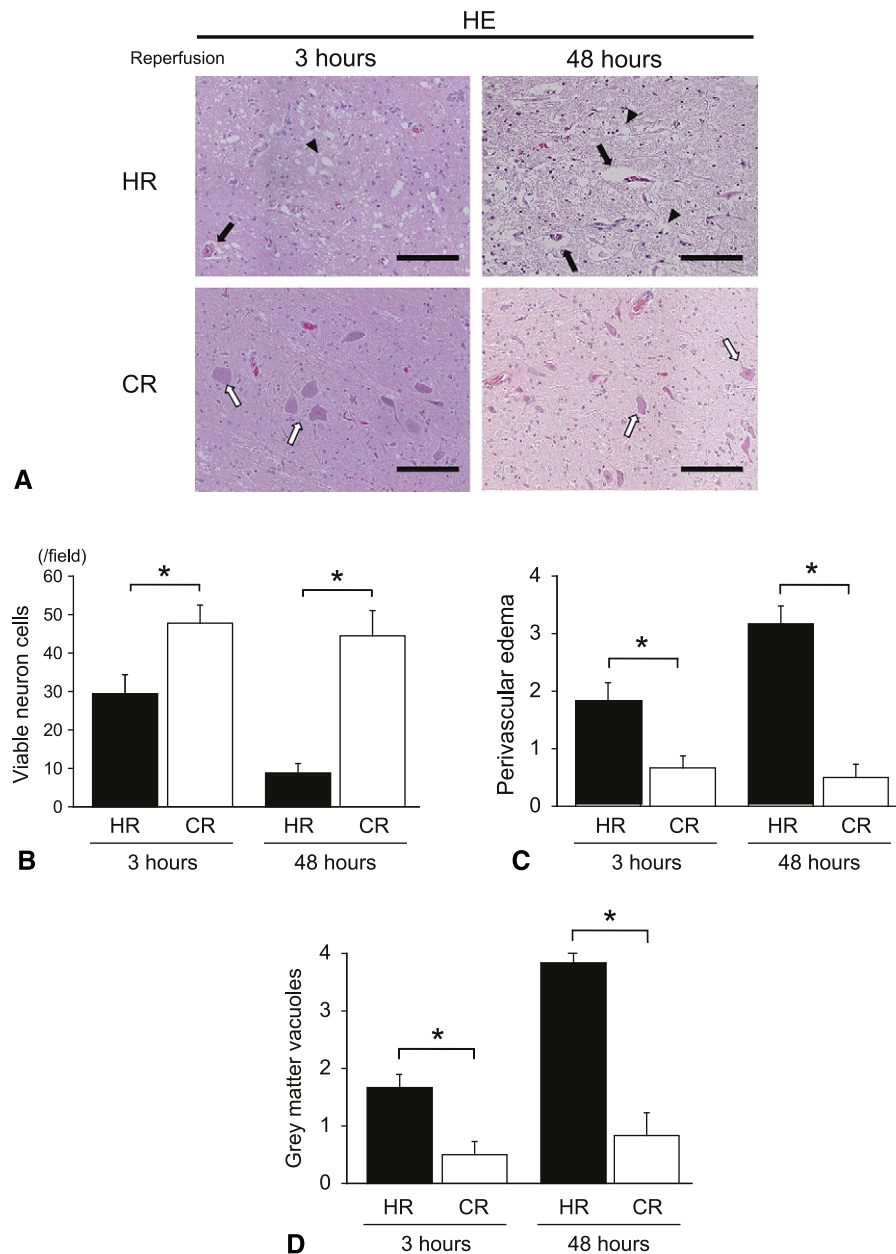
FIGURE 3. Postoperative histologic assessment. A, Hematoxylin–eosin staining in the ventral gray matter of spinal cord at 3 and 48 hours of reperfusion. Photomicrographs of sections show viable neuron cells (*white arrows*), perivascular edema (*black arrows*), and gray matter vacuoles (*black arrowheads*). Bar = 200 μm. Quantitative analyses of viable neuron cells (B), perivascular edema (C), and gray matter vacuoles (D). *$P < .05$. All data are expressed as means $\pm$ SEM for n = 6 rabbits. *$P < .05$. *HE,* Hematoxylin-eosin; *HR,* high BP group; *CR,* control BP group.

evaluated the effect of a similarly high BP (120 mm Hg) during SCR on simple reperfusion injury under minimal ischemic insult.

This study demonstrated that a high mean BP of 120 mm Hg ($\sim>1.5$ times the normal) in the early phase of reperfusion has disadvantageous effects on the spinal cord, in contrast with beneficial effects of a high BP during SCI in our previous study.[2] Because the normal mean BP in conscious rabbits ranged from 64.4 to 66.0 mm Hg in our

previous model,[2] the 120-mm Hg BP in rabbits might correspond to excessively high BP in humans. In neurologic assessment, the high BP in the early phase of SCR caused a slow and incomplete Tc-MEP recovery followed by a decreased modified Tarlov score at 3 hours of reperfusion. Neurologic events after aortic surgery are well known as 2 chronologically distinct entities: early- or delayed-onset neurologic deficit. An early-onset deficit is recognized immediately after operation, whereas a delayed deficit
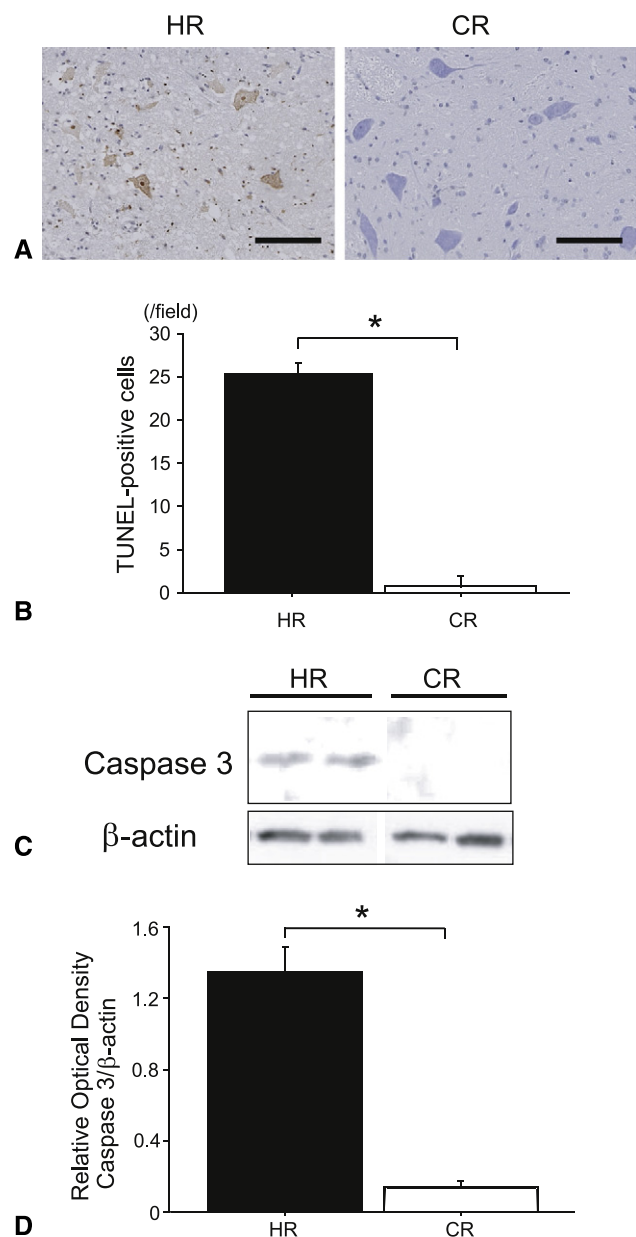
FIGURE 4. Postoperative evaluation of spinal cord apoptosis. A, TUNEL staining of the ventral gray matter of spinal cord at 48 hours of reperfusion. Photomicrographs of sections show TUNEL-positive cells (*brown*). Bar = 200 μm. B, Quantitative analysis of TUNEL-positive neuron cells at 48 hours of reperfusion. C, Western blot analysis of caspase 3. D, Relative OD of caspase 3 in each group. All data are expressed as means ± SEM for n = 6 rabbits. *P < .05. *TUNEL,* Terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling; *HR,* high BP group; *CR,* control BP group.

develops anytime after 1 day postoperatively.[14] Our results suggest that the high BP in the early phase of SCR may be related to the exacerbation of early-onset paraplegia.

Tc-MEPs reflect the functional integrity of motor neuron pathways and promptly respond to ischemia in the spinal cord. Tc-MEPs disappear soon after SCI and recover to a cer-tain level during SCR. Our previous study demonstrated that the recovery ratio of tc-MEP amplitude is positively correlated to the MTS and the number of viable neuron cells in the anterior horn of the spinal cord.[7] In this study, the recovery ratio of tc-MEPs in the HR group was significantly lower than in the CR group. This precise profile of tc-MEPs is one of the strong pieces of evidence that high BP in the early phase of SCR may be associated with the incidence of postoperative paraplegia. Notably, tremor of the hind limbs was observed in the early phase of reperfusion in almost all cases in the HR group, and the degradation of tc-MEP was observed after its maximal recovery in some cases in the HR group. These findings in the early phase of reperfusion may be important. However, further studies of tc-MEPs are needed throughout the SCR period.

In histologic assessment, there were fewer viable neuron cells and more TUNEL-positive cells in the anterior horn of the spinal cord in the HR group compared with the CR group. To further evaluate spinal cord apoptosis, we performed Western blotting of caspase 3. Ischemia by itself can trigger apoptosis and reperfusion accelerates the process,[15] and apoptosis has been shown to be an important mode of earlier neuronal damage in the spinal cord after ischemic insults.[16] This study shows that the neurologic score at 48 hours was worse than at 3 hours and that apoptosis was significantly more severe at 48 hours, suggesting that the acceleration of spinal cord injury may have been mainly caused by apoptosis.

Microscopic neuron cell damage by BP augmentation has also been shown as perivascular edema and gray matter vacuolation in this study. Because reperfusion in a form of hyperperfusion induces secretion of more inflammatory and vasodilatory substances, such as bradykinin, arachidonate, and superoxides,[17] those findings might be the result of reperfusion hyperemia and free radical generation. Early reperfusion injury triggers an endothelial barrier dysfunction, characterized by neutrophil infiltration and increased vascular permeability caused by oxidative stress.[12] The present study showed that the high BP in the early phase of SCR promoted an oxidative inflammatory cascade involving the enhancement of vascular permeability, MPO activity, and superoxide generation. These findings suggest that increased oxidative stress by the BP augmentation in the early phase of SCR may contribute to the mechanism of early-onset paraplegia.

It is generally believed that systemic hypotension has adverse effects on delayed paraplegia after aortic surgery, whereas systemic[18-21] hypertension has an effective role. Our previous clinical research also demonstrated that the duration of hypotension after weaning from bypass was an independent risk factor for paraplegia in patients undergoing thoracoabdominal aortic repair.[22] However, Shi and colleagues[6] reported that low-pressure perfusion for 10 minutes at the beginning of reperfusion attenuated neurologic deficits

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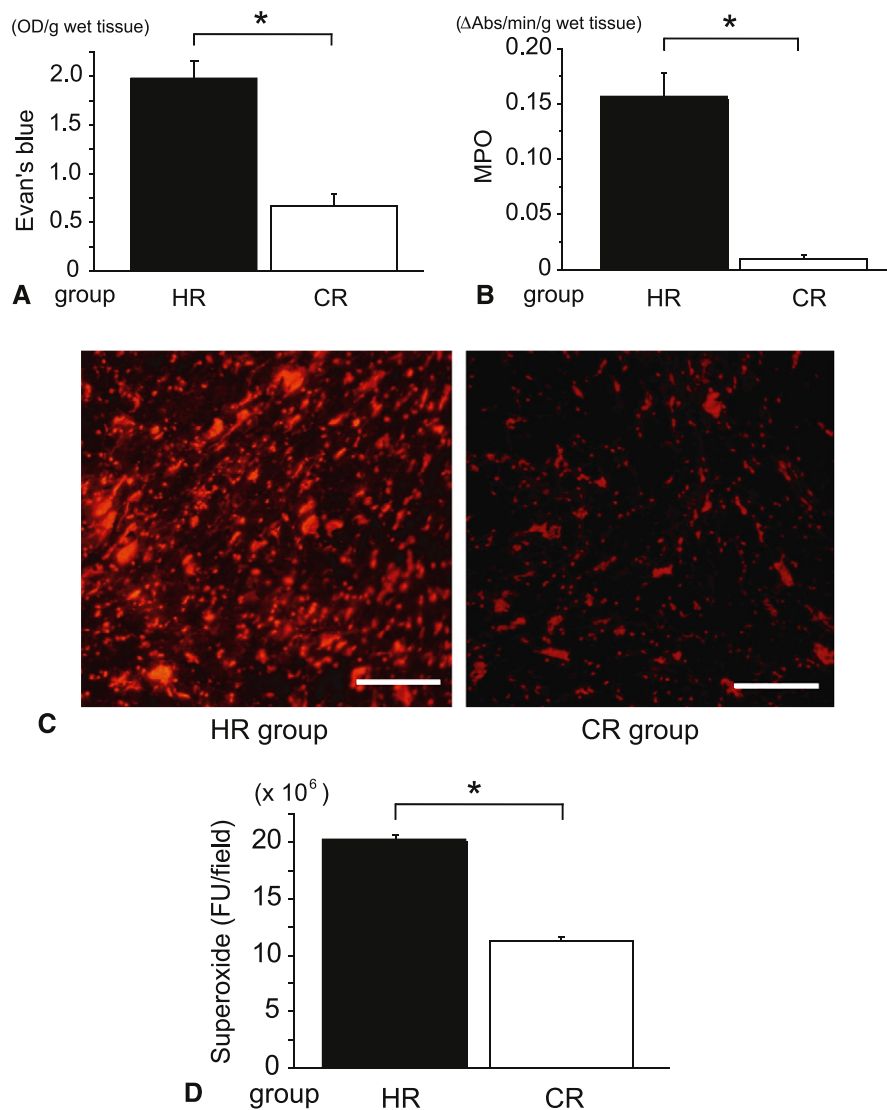
FIGURE 5. Early reperfusion injury in the spinal cord at 3 hours of reperfusion. A, Vascular permeability. B, MPO activity. *ΔAbs* indicates a change in absorbance. C, In situ detection of superoxide generation (*red fluorescence*). Bar = 200 μm. D, Semiquantitative analysis of the superoxide generation. All data are expressed as means ± SEM for n = 6 rabbits. *P < .05. *OD,* Optical density; *MPO,* myeloperoxidase; *FU,* fluorescence unit; *HR,* high BP group; *CR,* control BP group.

after ischemia. Furthermore, we showed that high-pressure perfusion for 15 minutes in the early phase of reperfusion exacerbated neurologic deficits in the present study. These discrepancies in the effects of controlled BP during SCR on spinal cord injury seem to be associated with the timing and duration of the controlled BP. We believe that both avoidance of reperfusion injury and maintenance of optimal blood flow to the spinal cord during reperfusion are crucial factors to prevent postischemic paraplegia. Therefore, excessively high BP should be avoided in the early phase of reperfusion, but sufficient BP for spinal cord blood flow may be required during reperfusion. Further investigation is necessary to elucidate the relationship between the BP management during reperfusion and the spinal cord injury in aortic surgery.

We have reported that the proximal mean arterial pressure was clinically maintained between 60 and 100 mm Hg and that the distal perfusion pressure was kept at more than 70 mm Hg during aortic crossclamping.[2,22] By taking the idea from this study and relating it to the clinical setting, excessive BP augmentation immediately after aortic unclamping, particularly when reconstructing the intercostal or lumbar pivotal arteries (which has the potential to provide excessive blood flow), might worsen the early reperfusion injury in aortic surgery. Our previous study indicated that BP augmentation by distal aortic perfusion using left-sided heart bypass or partial cardiopulmonary bypass during SCI caused by aortic crossclamping may decrease the incidence of spinal cord injury after paraplegia.[22] Because the increased

collateral blood flow solely maintains a sufficient blood supply to the spinal cord during aortic clamping, BP augmentation during SCI should be important in protecting the spinal cord. BP augmentation during SCR might not only increase direct blood flow through the reconstructed intercostal arteries but also increase collateral flow to the spinal cord, boosting the reperfusion injury. Subsequently, avoidance of SCR with high BP immediately after aortic unclamping might create a more sophisticated protection of the spinal cord in aortic surgery.

Study Limitations

The rabbit SCI model had less ischemic injury with a high BP during the SCI, according to our previous study.[2] This model enabled the discovery of a potential management strategy to better protect the spinal cord in aortic surgery. The conditions of this model, including the duration and level of BP during the SCI or SCR, were determined according to the previous study. Therefore, the optimal duration or level of BP during the SCR was not evaluated in the present study. There are some differences in vascular anatomy and clinical response to the SCI and SCR between rabbits and humans. In rabbits, there are some collaterals from pial anastomoses via the posterior spinal artery to the lumbar cord, but the caudal blood flow is mainly from the segmental arteries.[23] On the other hand, there are many collaterals from the lumbar and internal iliac arteries via the anterior spinal artery to the caudal spinal cord in humans.[23,24] We did not completely assess the delayed-onset neurologic deficit in the present study. Although there seems to be a main concern that pharmacologic intervention with phenylephrine may have produced severe vasoconstriction that leads to SCI by constricting the arteries supplying the spinal cord, our previous study[2] demonstrated that the mean BP of 120 mm Hg induced by phenylephrine did not alter the spinal cord blood flow compared with preintervention. In addition, Lindsberg and colleagues[25] reported that pharmacologic infusion of phenylephrine does not constrict spinal arteries severely enough to produce SCI.

CONCLUSIONS

High BP in the early phase of SCR deteriorated early reperfusion injury in the spinal cord, leading to exacerbation of early-onset paraplegia in rabbits. The present study suggests that it may be important to avoid excessive BP augmentation immediately after aortic unclamping for spinal cord protection and that totally coordinated BP management during both SCI and SCR may reduce postoperative neurologic complications in thoracoabdominal aortic surgery.

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