

8. T. Komatsu, Y. Oguro, A. Nakagawa, E. Tsuchida. Albumin clusters: structurally defined protein tetramer and oxygen carrier including thirty-two iron(II) porphyrins. *Biomacromolecules* **6**, 3397–3403 (2005).
 9. A. Nakagawa, T. Komatsu, M. Iizuka, E. Tsuchida. Human serum albumin hybrid incorporating tailed porphyrinatoiron(II) in the $\alpha, \alpha, \alpha, \beta$ -conformer as an O₂-binding site. *Bioconjugate Chem.* **17**, 146–151 (2005).
 10. H. Sakai, H. Horinouchi, M. Yamamoto, E. Ikeda, S. Takeoka, M. Takaori, E. Tsuchida, K. Kobayashi. Acute 40% exchange transfusion with Hb-vesicles (HbV) suspended in recombinant HSA solution: Degradation of HbV and erythropoiesis in rat spleen observed for 2 Weeks. *Transfusion* **46**, 339–347 (2006).
 11. H. Abe, M. Fujihara, H. Azuma, H. Ikeda, K. Ikebuchi, S. Takeoka, E. Tsuchida, H. Harashima. Interaction of hemoglobin vesicles, a cellular-type artificial oxygen carrier, with human plasma: effects on coagulation, kallikrein-kinin, and complement systems. *Artif. Cells Blood Substit. Immobil. Biotechnol.* **34**, 1–10 (2006).
 12. Y. Huang, T. Komatsu, R.-M. Wang, A. Nakagawa, E. Tsuchida. Poly(ethylene glycol) Conjugated Human Serum Albumin Including Iron Porphyrins: Surface Modification Improves the O₂-Transporting Ability. *Bioconjugate Chem.* **17**, (2006) in press
 13. H. Sakai, H. Horinouchi, E. Tsuchida, K. Kobayashi. One-year observation of Wistar rats after infusion of Hb-vesicles (Artificial oxygen carriers). *Artif. Cells Blood Substitutes Biotechnol.* (2006) in press.
- (総説、著書など)
1. 酒井宏水、宗慶太郎、武岡真司、小林絃一、土田英俊. 人工赤血球. 「医療用マテリアルと機能膜」第5章、pp 107-118, 榊シーエムシー出版, 2005.
 2. 酒井宏水、土田英俊、目でみるバイオ「微小血管内を均一に流れる人工赤血球とその運命」、バイオサイエンスとインダストリー **63**, 571-572 (2005)
 3. 土田英俊、酒井宏水、小松晃之、小林絃一、酸素輸液(人工赤血球)の臨床応用、先端医療シリーズ **37** 「人工臓器・再生医療の最先端」第16章-4. pp. 279-286, 2005 寺田国際事務所 / 先端医療技術研究所
 4. 土田英俊、小林絃一、(トピックス)輸血製剤への新しい取り組み：人工赤血球、麻酔科診療プラクティス **18**. 周術期の輸液・輸血療法, pp. 270-273, 2005 文光堂
 5. H. Sakai, K. Sou, S. Takeoka, K. Kobayashi, and E. Tsuchida, “Hemoglobin-Vesicles as a Molecular Assembly: Characteristics of Preparation Process and Performances as Artificial Oxygen Carriers.” In “Blood Substitutes” (Ed. By Robert M. Winslow, Elsevier), Chapt. 44, pp. 514-522, 2006.
 6. T. Komatsu, Y. Huang, H. Yamamoto, H. Horinouchi, K. Kobayashi, E. Tsuchida. “Albumin- heme: a synthetic heme-based oxygen carrier”. In “Blood Substitutes” (Ed. By Robert M. Winslow, Elsevier), Chapt. 46, pp. 532–539, 2006.
 7. A.G. Tsai, P. Cabrales, H. Sakai, and M. Intaglietta. “Blood Substitutes' Efficacy: Microvascular and Theological Determinants.” In: *Microvascular Research: Biology and Pathology*, Vol. 2. (Ed: David Shepro), San Diego: Elsevier, 2006, pp. 1095-1103.
 8. H. Sakai, E. Tsuchida. Performances of PEG-modified hemoglobin-vesicles as artificial oxygen carriers in microcirculation. *Clin. Hemorheol. Microcirc.* **34**, 335-340 (2006).
 9. E. Tsuchida, H. Sakai, H. Horinouchi, K. Kobayashi. Hemoglobin-vesicles as a transfusion alternative. *Artif. Cells Blood Substitutes Biotechnol.* (2006), in

press.

2. 学会発表

1. 宗慶太郎、B. Goins, W.T. Phillips, 酒井宏水、武岡真司、土田英俊／人工赤血球(ヘモグロビン小胞体)の血中半減期と代謝臓器への分布過程／2005.5.25-27／パシフィコ横浜
2. 酒井宏水、宗慶太郎、武岡真司、堀之内宏久、小林紘一、土田英俊／人工赤血球(ヘモグロビン小胞体)大量投与後の細網内皮系における代謝過程／第54回高分子学会年次大会／2005.5.25-27／パシフィコ横浜
3. 酒井宏水、D. Erni, M. Intaglietta, 土田英俊／人工赤血球(ヘモグロビン小胞体)による虚血領域酸素化の機序解明／第54回高分子学会年次大会／2005.5.25-27／パシフィコ横浜
4. 中川晶人、飯塚 誠、小松晃之、土田英俊／ $\alpha 3 \beta$ 置換ヘム誘導体を包接したアルブミン複合体の酸素結合能／第54回高分子学会年次大会／2005.5.25-27／パシフィコ横浜
5. 黄 宇彬、中川晶人、小松晃之、土田英俊／アルブミン-ヘムの表面修飾と物性・酸素結合の相関／第54回高分子学会年次大会／2005.5.25-27／パシフィコ横浜
6. R.-M. Wang, T. Komatsu, E. Tsuchida / New Albumin-heme conjugate covalently linked oxygen-binding sites / The 12th International Congress of Biorheology & The 5th International Conference on Clinical Hemorheology / 2005.5.30-6.3/ Chongqing, China.
7. Y. Huang, T. Komatsu, E. Tsuchida. / Structure, properties and oxygen-binding ability of polyoxyethylene-modified albumin-heme / The 12th International Congress of Biorheology & The 5th International Conference on Clinical Hemorheology / 2005.5.30-6.3/ Chongqing, China.
8. 酒井宏水、堀之内宏久、武岡真司、小林紘一、土田英俊／人工赤血球(ヘモグロビン小胞体)による血液希釈後の回復過程／第53回日本輸血学会総会／2005.5.26-28／東京ベイホテル東急
9. 酒井宏水、勢司泰久、佐藤夏枝、堀之内宏久、武岡真司、土田英俊、小林紘一／ヘモグロビン小胞体による50%出血ショック蘇生後の回復過程／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
10. 泉陽太郎、山本 学、竹内 健、渡辺真純、堀之内宏久、寺村裕治、酒井宏水、武岡真司、土田英俊、小林紘一／人工酸素運搬体ヘモグロビン小胞体による固形腫瘍の酸素化の試み／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
11. 酒井宏水、勢司泰久、堀之内宏久、池田栄二、武岡真司、土田英俊、小林紘一／ヘモグロビン小胞体の単回投与1年後の血液生化学、組織病理学的検討／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
12. 阿部英樹、東 寛、藤原満博、山口美樹、酒井宏水、武岡真司、土田英俊、池田久實／ヘモグロビン小胞体(HbV)がラット免疫系(脾臓細胞)に及ぼす影響／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
13. 山本 学、堀之内宏久、渡辺真純、酒井宏水、武岡真司、勢司泰久、佐藤夏枝、須賀裕子、小林紘一、土田英俊／ビーグル犬50%脱血ショックモデルにおけるHb小胞体の蘇生効果と安全性評価／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
14. 安楽 誠、浦田由紀乃、武岡真司、土田英俊、小田切優樹／マウスにおけるヘモグロビン小胞体の血中滞留性と組織移行性について／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
15. 宗慶太郎、武岡真司、土田英俊／ポリエチレングリコール鎖を結合した両親媒性化合物によるリン脂質小胞体の表面修飾とヘモグロビン小胞体の安定化効果／第12回日本血液代替物学会年

次大会／2005.6.6-7／東京 早稲田大学

16. 阿閉友保、相原源就、土田英俊、武岡真司／metHb/L-Tyrによる過酸化水素消去系を封入したヘモグロビン小胞体の機能評価／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
17. 藤原満博、若本志乃舞、阿部英樹、山口美樹、東 寛、武岡真司、土田英俊、池田久實／In vitroにおけるヘモグロビン小胞体の血小板活性化に対する影響
18. 武岡真司／分子集合科学を利用した人工血液の創製(大会長講演)／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
19. 小松晃之、土田英俊／部位特異的アミノ酸置換を利用した新しいアルブミン-ヘムの合成と酸素結合／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
20. 浦田由紀乃、安楽 誠、小松晃之、土田英俊／組換えアルブミン二量体の体内動態特性について／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
21. 中川晶人、王 榮民、黄 宇彬、小松晃之、土田英俊／ポリエチレングリコール鎖で表面修飾したアルブミン-ヘムの酸素結合／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
22. 黄 宇彬、小松晃之、中川晶人、王 榮民、土田英俊／ポリエチレングリコール鎖で表面修飾したアルブミン-ヘムの合成とその構造および溶液物性／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
23. 王 榮民、小松晃之、土田英俊／Synthesis and O₂-Binding Properties of Albumin-Heme Covalently Linked GluFePs as O₂-Coordination Site／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
24. 山本尚志、堀之内宏久、山本 学、小林紘一、小松晃之、中川晶人、黄 宇彬、弘津一郎、甲斐俊哉、土田英俊／麻酔下イヌ出血ショックモデルを用いた人工酸素輸液アルブミン-ヘムの酸素運搬能評価／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
25. 飯塚 誠、武岡真司、中川晶人、小松晃之、土田英俊／新規な酸素結合サイト $\alpha^3\beta$ 型ヘムの合成とアルブミン-ヘムの酸素結合／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
26. 佐藤高彰、中川晶人、小松晃之、土田英俊／アルブミン-ヘムの静的構造とダイナミクス／第12回日本血液代替物学会年次大会／2005.6.6-7／東京 早稲田大学
27. K. Kobayashi, H. Sakai, M. Yamazaki, M. Yamamoto, H. Horinouchi, S. Takeoka, R. Yozu, E. Tsuchida. / The efficacy of hemoglobin-vesicle, an artificial oxygen carrier, in hemorrhagic shock resuscitation, and cardiopulmonary bypass. / The 51st Annual Conference of American Society for Artificial Internal Organs (ASAIO). / 2005.6.9-11 / Washington DC
28. H. Sakai, P. Cabrales, A.G. Tsai, S. Takeoka, D. Erni, M. Intaglietta, E. Tsuchida / Oxygen releasing from Hb-vesicles in ischemic microcirculation / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
29. H. Sakai, Y. Seishi, N. Satoh, H. Horinouchi, S. Takeoka, E. Tsuchida, K. Kobayashi. / Fourteen days observation after resuscitation from hemorrhagic shock using Hb-vesicles suspended in recombinant albumin in a rat model. / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
30. J. Plock, C. Contaldo, H. Sakai, S. Takeoka, E. Tsuchida, D. Erni. / The role of hemoglobin encapsulated in liposome vesicles in the oxygenation of critically ischemic hamster flap tissue / 10th

- International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
31. H. Sakai, H. Horinouchi, M. Yamamoto, K. Sou, S. Takeoka, E. Tsuchida, K. Kobayashi. / Recovery after 40% exchange transfusion with Hb-vesicles suspended in recombinant albumin: physiological capacities for degradation of Hb-vesicles and hematopoiesis. / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 32. T. Atoji, M. Aihara, H. Sakai, E. Tsuchida, S. Takeoka. / Prolongation of oxygen carrying ability of hemoglobin-vesicles by hydrogen peroxide elimination using methemoglobin and L-tyrosine / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 33. H. Sakai, Y. Seishi, K. Ohta, H. Horinouchi, E. Ikeda, S. Takeoka, E. Tsuchida, K. Kobayashi / Histopathological and plasma biochemical analyses one year after bolus infusion of Hb-vesicles in Wistar rats. / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 34. M. Yamamoto, K. Kobayashi, H. Horinouchi, H. Yamamoto, H. Sakai, S. Takeoka, Y. Suka, E. Tsuchida. / Safety and effectiveness of hemoglobin vesicles in 50% hemorrhage shock model in dog / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 35. H. Sakai, P. Cabrales, A.G. Tsai, S. Takeoka, D. Erni, M. Intaglietta, E. Tsuchida / Oxygen releasing from Hb-vesicles in ischemic microcirculation / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 36. K. Sou, B. Goins, W.T. Phillips, H. Sakai, S. Takeoka, E. Tsuchida / Circulation kinetics and organ distribution of the hemoglobin-vesicles (HbV) / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 37. K. Kobayashi, H. Horinouchi, Y. Izumi, M. Watanabe, H. Yamamoto, R. Yozu, H. Sakai, T. Komatsu, Y. Huang, A. Nakagawa, S. Takeoka, and E. Tsuchida. / Preclinical studies of Hb-vesicles and albumin-hemes. / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 38. Y. Izumi, M. Yamamoto, K. Takeuchi, M. Watanabe, H. Horinouchi, Y. Teramura, H. Sakai, S. Takeoka, E. Tsuchida, K. Kobayashi / Systemic administration of hemoglobin vesicle augments radiation response in lewis lung carcinoma. / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 39. T. Komatsu, E. Tsuchida. / Human serum albumin having a prosthetic heme group in a tailor-made heme pocket / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 40. A. Nakagawa, T. Komatsu, E. Tsuchida. / O₂-binding properties of albumin-heme hybrid incorporating $\alpha_3\beta$ -substituted heme derivative / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 41. Y. Huang, T. Komatsu, R.M. Wang, E. Tsuchida. / Polyoxyethylene-modified albumin-heme hybrid: synthesis, property, oxygen-binding ability / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 42. R.M. Wang, T. Komatsu, E. Tsuchida. / Albumin-heme conjugate covalently attached heme sites / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 43. H. Yamamoto, H. Horinouchi, M. Yamamoto, K. Kobayashi, T. Komatsu, A. Nakagawa, Y. Huang, I. Hirotsu, T. Kai, E. Tsuchida. / Exchange transfusion with entirely synthetic red-cell substitute albumin-heme into anesthetized dogs: physiological responses and oxygen delivery / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
 44. H. Horinouchi, H. Yamamoto, T. Oba, M. Haraguchi,

- K. Kobayashi, T. Komatsu, E. Tsuchida. / Enhanced radiation response by using artificial oxygen carrier: albumin-heme (rHSA-FecycP). / 10th International Symposium on Blood Substitutes/ 2005.6.12-15/ Providence, RI/
45. F. Ma, D. Wang, S. Handa, K. Ogami, K. Umeda, T. Hekei, H. Sakai, E. Tsuchida, T. Nakahata, and K. Tsuji / Generation of functional hemoglobin-synthesizing erythroid cells from human embryonic stem cells. / 34th Annual Meeting of the International Society for Experimental Hematology (ISEH) / 2005.7.30-8.2 / Univ. Glasgow, UK.
46. 酒井宏水、武岡真司、小林絃一、土田英俊 / 人工赤血球(ヘモグロビン小胞体) / 第34回医用高分子シンポジウム / 2005. 8.1-2. / 東京、上智大学
47. H. Sakai, E. Tsuchida / Rheological property of hemoglobin-vesicles and the oxygen binding capacity (Invited lecture) / XIV International Material Research Congress / 2005. 8.21-25 / Cancun, Mexico
48. E. Tsuchida. / Safety and efficacy of oxygen-infusion as artificial red cells. (Invited Lecture) / IUPAC 11th International Symposium on Macromolecule-Metal Complexes / 10-13 Sept. 2005 / Pisa, Italy
49. T. Komatsu, E. Tsuchida. / Dioxygenation of human serum albumin having a prosthetic heme group in a tailor-made heme pocket. / IUPAC 11th International Symposium on Macromolecule-Metal Complexes / 10-13 Sept. 2005 / Pisa, Italy
50. E. Tsuchida, T. Komatsu. / The advances of oxygen-infusions (hemoglobin vesicles and albumin hemes). (Plenary Lecture) / 8th International Symposium on Polymers for Advanced Technologies / 12-16 Sept. 2005 / Budapest, Hungary
51. T. Komatsu, E. Tsuchida. / O₂ and CO binding ability of human serum albumin having a prosthetic heme group. / 8th International Symposium on Polymers for Advanced Technologies / 12-16 Sept. 2005 / Budapest, Hungary
52. 酒井宏水、土田英俊 / 人工赤血球(Hb小胞体)のレオロジー特性と酸素放出挙動 / 第54回 高分子討論会 / 2005.9.20-22 / 山形大学
53. 宗慶太郎、Beth Goins、William T. Phillips、武岡真司、土田英俊 / 表面修飾小胞体の体内動態特性 / 高分子討論会 / 第54回 高分子討論会 / 2005.9.20-22 / 山形大学
54. 阿閉友保、相原源就、武岡真司、土田英俊 / 活性酸素消去系の導入によるヘモグロビン小胞体の酸素運搬能向上 / 高分子討論会 / 第54回 高分子討論会 / 2005.9.20-22 / 山形大学
55. 鈴木大祐、武岡真司、宗慶太郎、土田英俊 / 気液界面光反応を効率化した装置を用いたヘモグロビン小胞体の配位子交換 / 第54回 高分子討論会 / 2005.9.20-22 / 山形大学
56. 中川晶人、小松晃之、土田英俊 / 遺伝子組換えアルブミン-プロトヘム複合体の酸素結合能 / 第54回 高分子討論会 / 2005.9.20-22 / 山形大学
57. 土田英俊 / 医療現場で利用できる酸素輸液(人工赤血球)はここまで来ている / ヒューマンライフサイエンスフォーラム2005 / 2005.10.21 / インテックス大阪
58. E. Tsuchida / Oxygen infusions (artificial oxygen carriers): Hb-vesicles and albumin-hemes. / TEDA-Bioforum / 2005. 11.. 3-6 / Teda, Tianjin, China.
59. 酒井宏水、堀之内宏久、小林絃一、土田英俊 / 人工赤血球(ヘモグロビン小胞体)の代謝過程における脾臓微小循環の動的解析 / 第43回 日本人工臓器学会大会 / 2005.11.30 - 12.2 / 東京・日本都市センター
60. 小林絃一、堀之内宏久、酒井宏水、土田英俊 / 人工赤血球製剤(ヘモグロビン小胞体)の臨床試験に向けて / 第43回 日本人工臓器学会大会 / 2005.11.30 - 12.2 / 東京・日本都市センター

61. 相原源就、阿閉友保、武岡真司、土田英俊/L-チロシン/メトヘモグロビン共封入ヘモグロビン小胞体のin vitro、in vivo評価/第43回 日本人工臓器学会大会/2005.11.30 - 12.2/東京・日本都市センター
62. 土田英俊/人工血液開発研究の経緯と近未来の展望/厚生労働科学研究 平成17年度研究成果発表会「人工血液をつくる(6)」/2006.2.11/日本科学未来館
63. 佐藤敦、酒井宏水、武岡真司、土田英俊/ストップフロー法によるヘモグロビン小胞体のNO、CO結合反応の解析/日本化学会第86春季年会/2006.3.27 - 30/日本大学理工学部船橋キャンパス
64. 阿閉友保、相原源就、武岡真司、土田英俊/L-チロシンによるフェリルヘモグロビン還元反応の解析(1)/日本化学会第86春季年会/2006.3.27 - 30/日本大学理工学部船橋キャンパス
65. 谷田海博孝, 阿閉友保, 武岡真司, 土田英俊, “L-チロシンによるフェリルヘモグロビン還元反応の解析(2)/日本化学会第86春季年会/2006.3.27 - 30/日本大学理工学部船橋キャンパス
66. 飯塚 誠、中川晶人、小松晃之、武岡真司、土田英俊/アルブミン-ヘム複合体の酸素結合に及ぼすポルフィリン構造の効果/日本化学会第86春季年会/2006.3.27 - 30/日本大学理工学部船橋キャンパス
67. 黄 宇彬、王 榮民、小松晃之、中川晶人、土田英俊/ポリエチレングリコール鎖で表面修飾したアルブミン-ヘムの特徴と酸素結合/日本化学会第86春季年会/2006.3.27 - 30/日本大学理工学部船橋キャンパス

3. 報道

Chemistry World, 12, 18 (2005), December, Royal Society of Chemistry, “Albumin complex engineered for artificial blood”

H. 知的財産権の出願・登録状況

「血中微粒子製剤の除去装置」(特願2005-152284).

別添 5

表 研究成果の刊行に関する一覧表

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>Ann. Thorac. Surg.</i> 81 , 1146-7 (2006). “Total cavopulmonary connection: Open anastomosis of an extracardiac conduit with vacuum-assisted venous drainage.”	2006 年	Elsevier	R. Aeiba R. Yozu M. Morita T. Matayoshi
<i>J. Vasc. Surg.</i> 42 , 765-71 (2005). “Protective use of N-methyl-D-aspartate receptor antagonists as a spinoplegia against excitatory amino acid neurotoxicity.”	2005 年	Mosby	Y. Cho T. Ueda A. Mori H. Shimizu Y. Haga R. Yozu
<i>Int. J. Cardiol.</i> 102 , 39-45 (2005). “Serum C-reactive protein elevation predicts poor clinical outcome in patients with distal type acute aortic dissection: association with the occurrence of oxygenation impairment.”	2005 年	Elsevier Scientific Publishers	Y. Sugano T. Anzai T. Yoshikawa T. Satoh S. Iwanaga T. Hayashi Y. Maekawa H. Shimizu R. Yozu S. Ogawa
ハートナーシング, 18 , 965-969 (2005). “人工赤血球(人工酸素運搬体)の臨床応用”	2005 年	メディカ出版	小林絃一 山崎真敬 饗庭了 四津良平 土田英俊
「心臓外科 Knack & Pitfalls 弁膜症外科の要点と盲点」高本眞一 監修、四津良平 編集、p103-5. 2005 文光堂, “Ross 手術: 自己肺動脈弁を用いた大動脈弁置換術”	2005 年	文光堂	饗庭了
<i>J. Infect. Chemother.</i> 11 , 278-87 (2005). “Current status of diagnosis and treatment of invasive fungal infections in Japan: the influence of the new Japanese guidelines.”	2005 年	Springer-Verlag Tokyo	N. Aikawa S. Kohno K. Shibuya Y. Takesue S. Maesaki M. Yoshida I. Tokimatsu

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>J. Cardiovasc. Pharmacol.</i> 46 , 810-6 (2005). “Flow-independent myocardial ischemia induced by endothelin-1: an NADH fluorescence analysis.”	2005 年	Lippincott Williams & Wilkins	S. Inoue S. Hori T. Adachi K. Miyazaki S. Kyotani K. Fukuda H. Mori H. Nakazawa N. Aikawa S. Ogawa
<i>Ther. Apher. Dial.</i> 9 , 423-8 (2005). “Heat stroke with multiple organ failure treated with cold hemodialysis and cold continuous hemodiafiltration: a case report.”	2005 年	Blackwell Publishing, Asia Pty Ltd.,	S. Wakino S. Hori T. Mimura S. Fujishima K. Hayashi H. Inamoto T. Saruta N. Aikawa
<i>Int. Heart J.</i> 46 , 543-50 (2005). “A case of severe heat stroke with abnormal cardiac findings.”	2005 年	International Heart Journal Association	S. Wakino S. Hori T. Mimura S. Miyatake S. Fujishima N. Aikawa
<i>J. Infect. Chemother.</i> 11 , 152-9 (2005). “Multicenter prospective study of procalcitonin as an indicator of sepsis.”	2005 年	Springer-Verlag Tokyo	N. Aikawa S. Fujishima S. Endo I. Sekine K. Kogawa Y. Yamamoto S. Kushimoto H. Yukioka N. Kato K. Totsuka K. Kikuchi T. Ikeda K. Ikeda K. Harada S. Satomura

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>Burns</i> . 31, 331-6 (2005) “Prognostic implications of inhalation injury in burn patients in Tokyo.”	2005 年	Elsevier	M. Suzuki N. Aikawa K. Kobayashi R. Higuchi
<i>J Emerg Med</i> . 28, 237-41 (2005). “Review. Emergency medical services in Japan: an opportunity for the rational development of pre-hospital care and research.”	2005 年	Elsevier	M. R. Lewin S. Hori N. Aikawa
<i>Burns</i> . 31 Suppl 1, S3-S11 (2005). “Epidemiological and outcome characteristics of major burns in Tokyo.”	2005 年	Elsevier	K. Kobayashi H. Ikeda R. Higuchi M. Nozaki Y. Yamamoto M. Urabe S. Shimazaki A. Sugamata N. Aikawa N. Ninomiya H. Sakurai Y. Hamabe N. Yahagi H. Nakazawa
<i>Am. J. Physiol. Heart Circ. Physiol</i> 288, H1885-H1892 (2005). “Oxygen transport by low and normal P ₅₀ Hb-vesicles in extreme hemodilution.”	2005 年	American Physiological Society	P. Cabrales H. Sakai A. G. Tsai S. Takeoka E. Tsuchida M. Intaglietta
<i>Crit. Care Med</i> . 33, 806-812 (2005). “New generation of hemoglobin-based oxygen carriers evaluated for oxygenation of critically ischemic hamster flap tissue.”	2005 年	American Thoracic Society	C. Contaldo J. Plock H. Sakai S. Takeoka E. Tsuchida M. Leuing A. Banic D. Erni

刊行書籍又は雑誌名 (雑誌のときは雑誌名、巻号数、論文名)	刊行年月日	刊行書店名	執筆者名
<i>Am. J. Physiol. Heart Circ. Physiol.</i> 288 , H2897-H2903 (2005). "Oxygen Release from low and normal P50 Hb-vesicles from Transiently Occluded Arteriole in the Hamster Window Model."	2005 年	American Physiological Society	H. Sakai P. Cabrales A. G. Tsai M. Intaglietta E. Tsuchida
<i>Am. J. Physiol. Heart Circ. Physiol</i> 289 , H2624-H2631 (2005). "Is the Hb in Hb-vesicles infused for isovolemic hemodilution necessary to improve oxygenation in critically ischemic hamster skin?"	2005 年	American Physiological Society	J. A. Plock C. Contaldo H. Sakai E. Tsuchida M. Leunig A. Banic M. D. Menger D. Erni
<i>Artif Cells Blood Substit. Immobil. Biotechnol.</i> 33 , 101-11 (2005). "Effects of hemoglobin vesicles on resting and agonist-stimulated human platelets in vitro."	2005 年	Taylor & Francis, Inc.	S. Wakamoto M. Fujihara H. Abe M. Yamaguchi H. Azuma H. Ikeda S. Takeoka E. Tsuchida
<i>Bioconjugate Chem.</i> 16 , 23-26 (2005). "Human serum albumin bearing covalently attached iron (II) porphyrins as O ₂ -binding sites".	2005 年	American Chemical Society	R. M. Wang T. Komatsu A. Nakagawa E. Tsuchida
<i>J. Am. Chem. Soc.</i> 127 , 15933-15942 (2005). "O ₂ and CO binding properties of artificial hemoproteins formed by complexing iron protoporphyrin IX with human serum albumin mutants".	2005 年	American Chemical Society	T. Komatsu N. Ohmichi A. Nakagawa P. A. Zunszain S. Curry E. Tsuchida
<i>Biomacromolecules</i> 6 , 3397-3403 (2005). "Albumin clusters: structurally defined protein tetramer and oxygen carrier including thirty-two iron (II) porphyrins".	2005 年	American Chemical Society	T. Komatsu Y. Oguro A. Nakagawa E. Tsuchida

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>Bioconjugate Chem</i> 17146-151 (2005). “Human serum albumin hybrid incorporating tailed porphyrinatoiron(II) in the $\alpha,\alpha,\alpha,\beta$ -conformer as an O ₂ -binding site”.	2005 年	American Chemical Society	A. Nakagawa T. Komatsu M. Iizuka E. Tsuchida
<i>Bioconjugate Chem.</i> 17, (2006) in press “Poly (ethylene glycol) Conjugated Human Serum Albumin Including Iron Porphyrins: Surface Modification Improves the O ₂ -Transporting Ability.”	2006 年	American Chemical Society	Y. Huang T. Komatsu R. M. Wang A. Nakagawa E. Tsuchida
<i>Artif. Cells Blood Substitutes Biotechnol.</i> 34, 1-10 (2006). “One-year observation of Wistar rats after infusion of Hb-vesicles (Artificial oxygen carriers).”	2006 年	Taylor & Francis, Inc.	H. Abe M. Fujihara H. Azuma H. Ikeda K. Ikebuchi S. Takeoka E. Tsuchida H. Harashima
「医療用マテリアルと機能膜」第 5 章、pp 107-118, 2005. “人工赤血球 ”	2005 年 5 月	㈱シーエムシー出版	酒井宏水 宗 慶太郎 武岡真司 小林絃一 土田英俊
バイオサイエンスとインダストリー 63, 571-572 (2005). “目でみるバイオ「微小血管内を均一に流れる人工赤血球と その運命」 ”	2005 年	バイオインダストリー協会	酒井宏水 土田英俊
臨床麻酔 29, 721-726 (2005). “人工赤血球・人工血小板の開発の現状”	2005 年	真興交易(株)	武岡真司
「先端医療シリーズ 3 7 人工臓器・医療の最先端」第 16 章-4. pp. 279-286, 2005 “酸素輸液(人工赤血球)の臨床応用”	2005 年	寺田国際事務所 / 先端医療技術研究所	土田英俊 酒井宏水 小松晃之 小林絃一
「麻酔科診療プラクティス 18. 周術期の輸液・輸血療法」 pp. 270-273, 2005. “(トピックス)輸血製剤への新しい取り組み：人工赤血球”	2005 年 11 月	分光堂	土田英俊 小林絃一

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
In “ <i>Blood Substitutes</i> ” (Ed. By Robert M. Winslow), Chapt. 44, pp. 514-522, 2006. “Hemoglobin-Vesicles as a Molecular Assembly: Characteristics of Preparation Process and Performances as Artificial Oxygen Carriers.”	2006 年	Elsevier	H. Sakai K. Sou S. Takeoka K. Kobayashi E. Tsuchida
In “ <i>Blood Substitutes</i> ” (Ed. By Robert M. Winslow), Chapt. 46, pp. 532-539, 2006. “Albumin- heme: a synthetic heme-based oxygen carrier”.	2006 年	Elsevier	T. Komatsu Y. Huang H. Yamamoto H. Horinouchi K. Kobayashi E. Tsuchida
In: “ <i>Microvascular Research: Biology and Pathology</i> , Vol. 2.” (Ed: David Shepro), pp. 1095-1103, 2006. “Blood Substitutes' Efficacy: Microvascular and Theological Determinants.”	2006 年	Elsevier	A. G. Tsai P. Cabrales H. Sakai M. Intaglietta
<i>Clin. Hemorheol. Microcirc.</i> 34 , 335-340 (2006). “Performances of PEG- modified hemoglobin-vesicles as artificial oxygen carriers in microcirculation.”	2006 年	IOS Press	H. Sakai E. Tsuchida
<i>Transfusion</i> 46 , 339-347 (2006). “Acute 40% exchange transfusion with Hb-vesicles (HbV) suspended in recombinant HSA solution: Degradation of HbV and erythropoiesis in rat spleen observed for 2 weeks”	2006 年	American Association Of Blood Banks	H. Sakai H. Horinouchi M. Yamamoto E. Ikeda S. Takeoka M. Takaori E. Tsuchida K. Kobayashi
検査と技術 33 , 879-881 (2005). “人工酸素運搬体の開発 現状と将来展望.”	2005 年 9 月	Igaku-Shoin Ltd	堀之内宏久 泉 陽太郎 小林紘一 土田英俊
Annual Review 呼吸器 2005 , 152-155 (2005) “診断の進歩 細径気管支鏡”	2005 年	中外医学社	堀之内宏久 藤本博之 小林紘一

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>Reg. Anesth. Pain Med.</i> 30 , 464-72 (2005). “Neurotoxicity of intrathecally administered bupivacaine involves the posterior roots/posterior white matter and is milder than lidocaine in rats.”	2005 年	American Society of Regional Anesthesia and Pain Medicine	T. Takenami S. Yagishita S. Murase H. Hiruma T. Kawakami S. Hoka
<i>J. Anesth.</i> 19 , 208-12 (2005) “Patient-controlled epidural analgesia during labor using ropivacaine and fentanyl provides better maternal satisfaction with less local anesthetic requirement.”	2005 年	Springer Tokyo	M. Saito T. Okutomi Y. Kanai J. Mochizuki A. Tani K. Amano S. Hoka
<i>J. Anesth.</i> 19 , 106-11 (2005). “Noninvasive assessment of left ventricular pressure-area relationship using transesophageal echocardiography and tonometry during cardiac and abdominal aortic surgery.”	2005 年	Springer Tokyo	K. Yamaura S. Hoka H. Okamoto S. Takahashi
<i>Can. J. Anaesth.</i> 52 , 622-625 (2005). “Labour analgesia guided by echocardiography in a parturient with primary dilated cardiomyopathy.”	2005 年	Canadian Anaesthetists' Society	T. Okutomi M. Saito K. Amano K. Fukuoka S. Hoka
<i>Anal. Sci.</i> 21 , 337-9 (2005). “Determination of oxycodone and hydrocotarnine in cancer patient serum by high-performance liquid chromatography with electrochemical detection.	2005 年	The Japan Societyfor Analytical Chemistry	H. Kokubun M. Ouki M. Matoba H. Kubo S. Hoka K. Yago
<i>Can. J. Anaesth.</i> 52 , 281-4 (2005). “Rapid injection of epidural mepivacaine speeds the onset of nerve blockade.”	2005 年	Canadian Anaesthetists' Society	A. Kanai A. Suzuki S. Hoka

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>Neurosci Res.</i> 51 , 299-308 (2005). “Impaired acquisition of skilled behavior in rotarod task by moderate depletion of striatal dopamine in a pre-symptomatic stage model of Parkinson's disease.”	2005 年	Elsevier B.V	T. Ogura M. Ogata H. Akita S. Jitsuki L. Akiba K. Noda S. Hoka M. Saji
臨床麻酔 29 , 159-65 (2005). “内因性カンナビノイドの役割.”	2005 年	真興交易株式会社	外 須美夫
<i>Gene</i> 356 , 39-48 (2005). “Influence of inhalation anesthesia assessed by comprehensive gene expression profiling.”	2005 年	Elsevier B. V.	A. Sakamoto J. Imai A. Nishikawa E. Ito M. Yanagisawa R. Ogawa S. Watanabe
<i>Eur. J. Anaesthesiol.</i> 22 , 258-262 (2005) “Anesthesia and circulating blood volume.”	2005 年	European Society of Anesthesiology	Y. Sano A. Sakamoto Y. Oi R. Ogawa
<i>J. Nippon. Med. Sch.</i> 72 , 19-28 (2005). “Does carboxy- hemoglobin serve as a stress-induced inflammatory marker reflecting surgical insults?”	2005 年	Medical Association of Nippon Medical School	A. Sakamoto K. Nakanishi S. Takeda R. Ogawa
<i>J. Clin. Anesth.</i> 17 , 3-7 (2005). “Effects of atrial natriuretic peptide at a low dose on water and electrolyte metabolism during general anesthesia.”	2006 年	Elsevier Inc.	M. Koda A. Sakamoto R. Ogawa
<i>Anesth. Analg.</i> 100 , 294 (2005). “Successful management of tachycardiac atrial fibrillation in a septic with landiolol.”	2005 年	International Anesthesia Research society	Y. Yoshida T. Hongo A. Sakamoto R. Ogawa

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<p><i>Anesth. Analg.</i> 102, 233-236 (2006). “Unmasking of Brugada syndrome by an antiarrhythmic drug in a patient with septic shock.”</p>	2006 年	International Anesthesia Research society	K. Terajima T. Yamamoto H. Onodera S. Takeda K. Tanaka A. Sakamoto
<p><i>Shock</i>, 25, 184-189 (2006.) “Fluid resuscitation with Hemoglobin Vesicles in a rabbit model of acute hemorrhagic shock.”</p>	2006 年	Lippincott Williams & Wilkins	K. Terajima T. Tsueshita A. Sakamoto R. Ogawa
<p><i>Circ. J.</i> 69, 1035-1040 (2005) “Plasma matrix metalloproteinase-8 concentrations are associated with the presence and severity of coronary artery disease.”</p>	2005 年	Japanese Physiological Society	R. Kato Y. Momiyama R Ohmori H. Taniguchi H. Nakamura F. Ohsuzu
<p><i>Circ. J.</i> 69, 793-797(2005) “Polymorphism of the 3'-untranslated region of interleukin-12 p40 gene is not associated with the presence or severity of coronary artery disease.”</p>	2005 年	Japanese Circulation Society	Y. Momiyama R. Ohmori M. Nagano R. Kato H. Taniguchi T. Egashira H. Nakamura F. Ohsuzu
<p><i>Atherosclerosis</i> 81, 211-213 (2005). “Lack of any association between persistent hepatitis B or C virus infection and coronary artery disease.”</p>	2005 年	Elsevier	Y. Momiyama R. Ohmori R. Kato H. Taniguchi H. Nakamura F. Ohsuzu
<p><i>Am. J. Cardiol.</i> 95, 90-92 (2005) “Levels of matrix metalloproteinase-1 in patients with and without coronary artery disease and relation to complex and noncomplex coronary plaques.”</p>	2005 年	Excerpta Medica, Inc.,	R. Kato Y. Momiyama R. Ohmori H. Taniguchi H. Nakamura F. Ohsuzu

刊行書籍又は雑誌名（雑誌のときは雑誌名、巻号数、論文名）	刊行年月日	刊行書店名	執筆者名
<i>J. Atheroscler. Thromb.</i> 12, 53-60 (2005) “Characterization of the expression of TLR2 (Toll-like Receptor 2) and TLR4 on circulating monocytes in coronary artery disease.”	2005 年	Japan Atherosclerosis Society	K. Ashida K. Miyazaki E. Takayama H. Tsujimoto M. Ayaori T. Yakushiji N. Iwamoto A. Yonemura K. Isoda H. Mochizuki H. Hiraide M. Kusuhara F. Ohsuzu
<i>Atherosclerosis</i> 178, 173-177 (2005) “Associations of plasma C-reactive protein levels with the presence and extent of coronary stenosis in patients with stable coronary artery disease.”	2005 年	Elsevier	H. Taniguchi Y. Momiyama R. Ohmori A. Yonemura T. Yamashita S. Tamai H. Nakamura F. Ohsuzu

その他の刊行物

- 1) *Chemistry World*, 12, 18 (2005), Royal Society of Chemistry, “Albumin complex engineered for artificial blood”
- 2) 日刊工業新聞「血液型照合なしで大量使用 酸素輸液の用途に」(H17. 09. 26)
- 3) 日刊工業新聞「人工酸素運搬体 実証プラント建設 ニプロが 200規模」(H17. 10. 25)
- 4) 日刊工業新聞「大学発ベンチャーの挑戦 75 献血血液で酸素輸液 早慶のシーズ事業化」(H17. 12. 27)

研究成果の刊行物・別冊
(2005. 4. ～ 2006. 3.)

Total Cavopulmonary Connection: Open Anastomosis of an Extracardiac Conduit With Vacuum-Assisted Venous Drainage

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Insertion of a tube conduit for total cavopulmonary connection is sometimes technically demanding due to the crumpled stump of the inferior vena cava caused by a tourniquet of the inferior vena cava near the division line. Herein we describe an alternative in which the anastomosis is completed during removal of the tourniquet with the application of vacuum-assisted venous

drainage. This new technique may alleviate, if not completely eliminate, a concern associated with total cavopulmonary connection with extracardiac conduit in small patients.

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Total cavopulmonary connection using an extracardiac conduit technique has become one of the most commonly used modifications of Fontan-type operations [1, 2]. However, the insertion of a tube conduit is sometimes technically demanding due to the crumpled stump of the inferior vena cava (IVC) caused by a tourniquet of the IVC near the division line. We present a new technique using an open anastomosis of the IVC and a tube conduit with the application of vacuum-assisted venous drainage.

Technique

After general anesthesia is administered and the patient is prepared and draped, a midline sternotomy is performed. For patients with a previous bi-directional cavopulmonary shunt the pericardial adhesions are dissected only around the IVC and the neighboring right branch pulmonary artery. Cardiopulmonary bypass is established after cannulation of the ascending aorta, superior vena cava, and IVC. Straight and pliable venous cannula (Thin-Flex Single Stage Venous Drainage Cannula [Edwards Lifesciences LLC, Irvine, CA]) are used. The tip of the IVC venous cannula is positioned as usual, 2 cm below the diaphragm level. A tourniquet is applied to the IVC at the diaphragm level. The IVC is divided at the cavo-atrial junction, and the atrial stump is primarily closed by sutures. A slightly oversized polytetrafluoroethylene tube graft is selected and trimmed. Venous drainage is augmented with a vacuum-assisted negative pressure of between 40 and 60 mm Hg. An air bubble sensor is interposed in the venous drainage tube to recognize excessive air drawing, which could potentially

lead to air blockage of the tube. The tourniquet for the IVC is released in order to achieve an open anastomosis of the graft with the IVC. Essentially no venous blood is spilled from the IVC stump. The cardiotomy sucker tip is placed in the IVC lumen to further facilitate the bloodless anastomosis technique that is needed (Fig 1). The other end of the conduit is anastomosed to a transverse incision in the inferior aspect of the right branch pulmonary arterial wall. Again, vacuum-assisted venous drainage is potent enough to eliminate the need for vascular clamping of the pulmonary artery. Finally, cardiopulmonary bypass is terminated.

Comment

Extracardiac conduit total cavopulmonary connection has been increasingly accepted as the procedure of choice for modified Fontan operations, because the hemodynamic properties in the reconstructed systemic venous route are excellent, and the suture load on the atrial wall is minimal. These characteristics promise better long-term morbidity and mortality. As an increasing number of patients undergo total cavopulmonary connection at a younger age, a small-sized tube graft is inevitably implanted, although an over-sized tube graft is desirable for such growing patients. The conventional technique with a tourniquet of the IVC near the division line may result in a heavily crumpled IVC stump. This makes the end-to-end anastomosis technique of the IVC stump and the tube graft highly demanding, especially in cases with a significant size mismatch between the two. The open technique allows a full expansion of the IVC wall and the placement of the sucker in the IVC lumen, thus assuring the surgeon more precise suture performance in such a difficult situation.

The open technique with vacuum-assisted venous drainage has been used in adult patients undergoing cardiac transplantation with bi-caval anastomosis [3], in

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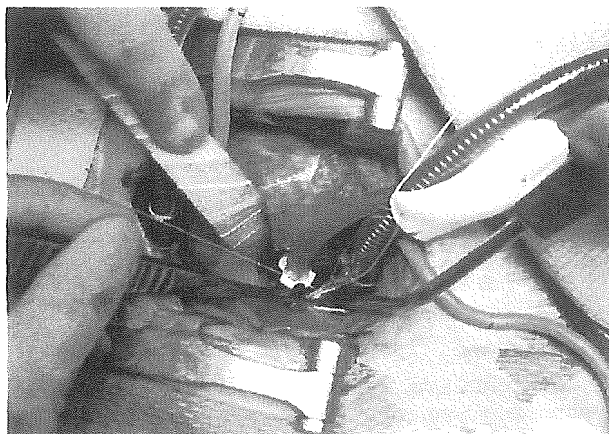


Fig 1. Surgeon's view of an open anastomosis with a tube graft and the inferior vena cava stump. Note a full expansion of the inferior vena cava wall and the placement of the sucker in the inferior vena cava lumen, thus assuring the surgeon's more precise suture performance.

which the IVC drainage was through the femoral vein. In our case, a direct IVC cannulation rather than peripheral venous drainage was used because of the small sizes that were involved. Our experience shows that direct IVC

cannulation does not necessarily exclude an open IVC technique. Potential drawbacks of this technique include air blockage of the circuit tube and failure to suck some of the hepatic venous blood. Each surgical team applying this technique should individualize the position and type of the IVC cannula to achieve optimal venous drainage.

In summary, open IVC anastomosis with vacuum-assisted venous drainage through direct access is a feasible, safe, and useful procedure even in pediatric patients. This new technique may alleviate, if not completely eliminate, a concern associated with extracardiac conduit total cavopulmonary connection in small patients.

References

1. Azakie A, McCrindle BW, Van Arsdell G, et al. Extracardiac conduit versus lateral tunnel cavopulmonary connections at a single institution: impact on outcomes. *J Thorac Cardiovasc Surg* 2001;122:1219-28.
2. Nakano T, Kado H, Ishikawa S, et al. Midterm surgical results of total cavopulmonary connection: clinical advantages of the extracardiac conduit method. *J Thorac Cardiovasc Surg* 2004;127:730-7.
3. Aklog L, Sepic J, Filsoofi F, Byrne JG, Adams DH. Open inferior vena caval anastomosis during bicaval heart transplantation. *Ann Thorac Surg* 2002;73:671-2.

Protective use of *N*-methyl-D-aspartate receptor antagonists as a spinoplegia against excitatory amino acid neurotoxicity

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Objective: Paraplegia remains a serious complication of thoracic and thoracoabdominal aortic operations. To avoid this dreadful complication, *N*-methyl-D-aspartate (NMDA) receptor antagonists have been examined in the ischemic or excitotoxic neuronal injury model. In the present study, we evaluated the protective efficacy of NMDA receptor antagonists that were infused segmentally after aortic clamping, as a spinoplegia, to reduce aspartate neurotoxicity in the spinal cord.

Methods: Infrarenal aortic isolation was performed in New Zealand white rabbits. Group A animals ($n = 7$) were pretreated with the segmental infusion of MK-801, a noncompetitive NMDA receptor antagonist, followed by segmental aspartate (50 mmol) infusion for 10 minutes. Group B animals ($n = 6$) received pretreatment with CGS19755, a competitive NMDA receptor antagonist, followed by the same aspartate infusion as group A. Group C animals ($n = 7$) received vehicle only, followed by aspartate infusion as a control group. In addition, group D animals ($n = 6$) were pretreated with MK-801 that was administered intravenously 1 hour before aspartate infusion. Neurologic status was assessed at 12, 24, and 48 hours after operation by using the Tarlov score. The spinal cords were procured at 48 hours for histopathologic analysis to determine the extent of excitotoxic neuronal injury.

Results: Most of the animals in groups A and D revealed full recovery or mild motor disturbance. Group B and C animals exhibited paraplegia or paraparesis with marked neuronal necrosis. In the Tarlov score at 48 hours, group A animals represented better neurologic function than group C ($P < .01$) and similar motor function to group D animals. Severe histopathologic change was not observed in groups A and D. Animals in groups A and D showed a greater number of motor neurons than animals in groups B and C ($P < .01$). The difference could be due to chance between group A and D animals ($P = .08$).

Conclusions: These results showed that the segmental infusion of noncompetitive NMDA receptor antagonist as an intraoperative spinoplegia could have a protective effect on the spinal cord neurons against excitotoxic neuronal injury in vivo. On the other hand, efficacy of the use of competitive antagonist was suggested to be limited in this model, probably because of the insurmountable obstacle of the blood-brain barrier. (J Vasc Surg 2005;42:765-71.)

Clinical Relevance: Paraplegia is a devastating complication during surgical repair of the thoracic and thoracoabdominal aortas. Excitatory amino acids neurotoxicity through the *N*-methyl-D-aspartate (NMDA) receptor is no doubt the pathologic hallmark of ischemic and posts ischemic spinal cord injury. Systemic administration of either a competitive or noncompetitive NMDA antagonist has been reported to have neuroprotective effect, in terms of preoperative treatment, with dose-related central sympathomimetic and sedative effects. Local administration, particularly of a noncompetitive NMDA antagonist, infused segmentally after aortic clamping could therefore be a potent intraoperative pharmacologic strategy to minimize the effective dose that retains NMDA antagonism without undesirable adverse effects. Our ability to reproduce this model could facilitate pharmacologic prevention or provide a new surgical technique as a spinoplegia for NMDA receptor-mediated neuronal injury.

Paraplegia is a devastating complication of surgical repair of the thoracic and thoracoabdominal aortas. The incidence varies between 1% and 30%, depending on the extent of the aneurysm, dissection, rupture, and aortic clamping time.¹⁻⁴ Surgical techniques, such as distal perfusion, hypothermia, spinal fluid drainage, and segmental repair of intercostal arteries, or protective pharmacologic strategies have been developed to reduce the occurrence of

this complication by either maintaining adequate spinal cord perfusion or increasing spinal cord ischemia tolerance.³⁻⁵ However, no method yet completely avoids this dreadful complication.

Excitatory amino acids (EAAs), mainly glutamate and aspartate, are major excitatory neurotransmitters in the central nervous system, including the spinal cord. EAAs are also well known to have neurotoxicity under metabolic stress in a manner of activating *N*-methyl-D-aspartate (NMDA) receptor and α -amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA) receptor.⁶⁻⁹ Many clinical and experimental reports have revealed that EAAs contribute to the irreversible and fatal neuronal injury during and after ischemia in the spinal cord; nevertheless, it has been difficult to indicate EAA neurotoxicity in vivo.¹⁰

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Competition of interest: none.

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