Analysis of Puncture Site-related Complications in Japanese Registry of Neuroendovascular Therapy (JR-NET)3

Masayuki SATO,1 Yuji MATSUMARU,1 Nobuyuki SAKAI,2 and on behalf of JR-NET study group affiliations

1Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan; 2Department of Neurosurgery and Comprehensive Stroke Center, Kobe City Medical Center General Hospital, Kobe, Hyogo, Japan

Abstract

A subgroup analysis of puncture site-related complications listed in the Japanese Registry of NeuroEndovascular Therapy 3, based on retrospective studies, was performed. Puncture site-related complications occurred in 315 (0.73%, average age: 65.2) of 36,708 patients out of all 43,303 registered cases. Carotid artery stenting (CAS, 95 patients, 1.1%, \( P < 0.01 \)) and extracranial percutaneous transluminal angioplasty (PTA, 21 patients, 1.4%, \( P < 0.01 \)) were associated with significantly higher incidence of puncture site-related complications. The incidence of complications correlated with the number of antiplatelet drugs (\( P < 0.001 \)). Although 40% of the puncture complications were treated conservatively, 13% were treated endovascularly and 5% underwent open surgery.

Key words: puncture-site related complication, endovascular treatment, nationwide survey

Introduction

Puncture site-related vascular complications occur in 3.1–9.7% of patients who underwent neuroendovascular therapy.1 Our previous data analysis from the Japanese Registry of Neuroendovascular Therapy (JR-NET)1 & 2 showed that access site complications occurred in 0.63% of all procedures.2 Retroperitoneal hematoma may result in death due to the massive bleeding. In recent years, hemostatic devices have been developed and improved, and showed efficacy in numerous meta-analyses, but retroperitoneal hematoma still requires much caution.1,3–5 In Japan, a prospective study on the access-site hemostatic device Angio-Seal (Terumo, Tokyo, Japan) proved its efficacy in neurondovascular therapy.6 JR-NET3 includes retrospectively registered studies on neuroendovascular therapy conducted by the Japanese Society for Neuroendovascular Therapy from January 2010 to December 2013. The registration parameters included disease-specific and cross-sectional parameters common in all diseases. In this article, puncture site-related vascular complications in JR-NET3 (a cross-sectional parameter) are analyzed.

Materials and Methods

Data of 36,708 patients out of all 43,303 cases registered in JR-NET3 were included in the evaluation. Puncture site-related complications included hemorrhagic complications, ischemic complications, and infections. If the hemostatic method was not described, it was not assessed. The presence or absence of an access site complication, age, sex, treatment facility (main hospital or satellite hospital), timing of surgery (scheduled or emergency), investigator (supervisor/specialist, or non-specialist), treatment (cerebral aneurysm embolization, arteriovenous malformation embolization, spinal lesion, dural arteriovenous fistula, intracranial tumor, carotid artery stenting (CAS), extracranial percutaneous transluminal angioplasty (PTA), intracranial PTA, acute recanalization therapy, spasm treatment, or other), outcome of complications (asymptomatic, transiently symptomatic, moderate disability, severe disability, or death), and the effect of complications on the treatment outcome were assessed. For puncture-related complications, we also examined how they were treated (conservative treatment, additional endovascular therapy, open...
surgery). Out of all patients who received treatment (cerebral aneurysm embolization, carotid artery stenting, extracranial PTA, and intracranial PTA), 25,348 cases with available data regarding antiplatelet therapy were included in the assessment of preoperative use of antiplatelet drugs. These variables were analyzed using Chi-square test for categorical variables and t-test for continuous variables, with a significance level of $P < 0.05$ (SPSS Ver. 22, IBM, Armonk, NY, USA) used in statistical analysis.

### Results

Puncture site-related complications occurred in 315 (0.73%) of all 43,303 cases (Table 1). Incidence of puncture site-related complications was not affected

| Table 1 Characteristics of puncture site-related complications |
|-----------------|---------------|---------------|---------------|----------------|---------------|
|                 | Total          | Complications (%) | Puncture site complication (%) | % In access site complication | Data unavailable | P-value |
| Patients        | 36708          | 3922 (10.7%)      | 315 (0.7)                 |                              | 0              |
| Cases           | 43303          | 3350 (9.7%)       | 269 (0.8)                 | 85.4                        | 52             | 0.57    |
| Age ± SD        | 65.2 ± 14.2    | 748              | 20 (0.9)                  | 6.3                         | 710            |
| Male            | 18,626 (50.7%) |                 |                           |                             |                |
| Facility        |                |                 |                           |                             |                |
| Main            | 34403          | 3350 (9.7%)       | 269 (0.8)                 | 85.4                        | 52             | 0.57    |
| Satellite       | 2253           | 572 (25.4)        | 20 (0.9)                  | 6.3                         |                |
| Timing          |                |                 |                           |                             |                |
| Schedule        | 24551          | 2396 (9.8)        | 193 (0.8)                 | 61.3                        | 40             | 0.84    |
| Emergency       | 12117          | 526 (4.3)         | 96 (0.8)                  | 30.5                        |                |
| Operator        |                |                 |                           |                             |                |
| Supervisor/Specialist | 34026      | 2023 (5.9)        | 301 (0.9)                 | 95.6                        | 718            | 0.43    |
| Non-specialist  | 1964           | 171 (8.7)         | 14 (0.7)                  | 4.4                         |                |
| Treatment       |                |                 |                           |                             |                |
| Aneurysm embolization | 17348    | 1803 (10.4)       | 140 (0.8)                 | 7.8                         | NS             |
| Aneurysm parent artery occlusion | 1315      | 260 (19.8)        | 8 (0.5)                   | 3.1                         | <0.01          |
| Arteriovenous malformation | 1456    | 128 (8.8)         | 1 (0.1)                   | 0.8                         | <0.01          |
| Spinal lesion   | 275            | 22 (8.0)          | 0                         | 0.0                         | NS             |
| Dural AVF       | 2776           | 129 (4.6)         | 4 (0.1)                   | 3.1                         | NS             |
| Tumour          | 1657           | 61 (3.7)          | 4 (0.1)                   | 6.6                         | NS             |
| Carotid artery stent | 8889      | 674 (7.6)         | 95 (1.1)                  | 14.1                        | <0.01          |
| Extracranial PTA | 1491      | 97 (6.5)          | 21 (1.4)                  | 21.6                        | <0.01          |
| Intracranial PTA | 1268      | 134 (10.6)        | 6 (0.5)                   | 4.5                         | NS             |
| Acute recanalization therapy | 3974   | 508 (12.8)        | 22 (0.6)                  | 4.3                         | <0.01          |
| Apasm           | 1804           | 42 (2.3)          | 0                         | 0.0                         | NS             |
| Other           | 1050           | 64 (6.1)          | 10 (1.0)                  | 15.6                        | (–)            |
| Outcome         |                |                 |                           |                             |                |
| Asymptomatic    | 78             | 24.8             |                           |                             |                |
| Transient symptom | 207       | 65.7             |                           |                             |                |
| Moderate disability | 12           | 3.8              |                           |                             |                |
| Severe disability | 10           | 3.2              |                           |                             |                |
| Dead            | 6              | 1.9              |                           |                             |                |
by the facility where operation was done, timing of operation, and the operator. Regarding the treatment, CAS (95 patients, 1.1%, \( P < 0.01 \)) and extracranial PTA (21 patients, 1.4%, \( P < 0.01 \)) were associated with a significantly higher incidence of complications, while parent artery aneurysm occlusion (one patient, 0.06%, \( P < 0.05 \)), arteriovenous malformation (one patient, 0.1%, \( P < 0.01 \)), and acute recanalization therapy (22 patient, 0.6%, \( P < 0.01 \)) were associated with a significantly lower incidence. The treatment for puncture site-related complications was conservative in 125 patients (40.0%), endovascular in 42 patients (13.3%), and open surgery in 16 patients (5.1%). The treatment outcome was asymptomatic or transiently symptomatic in 90.5% of patients, permanent disability in 22 patients (0.05%), and fatal in six patients (0.01%). The incidence of puncture site-related complications according to the use of antiplatelet drugs is shown in Figure 1. It was significantly different between the patients without therapy for complications (17 patients, 0.32%), those who received 1 or 2 drugs (202 patients, 1.16%), and those who received 3 or more drugs (28 patients, 1.47%). At the time of acute revascularization, combination of treatment with tissue plasminogen activator (tPA) had no effect on puncture site-related complications (0.6% with tPA vs 0.6% without tPA, \( P \)-value = 0.96; Table 2). In the carotid stent group, there was no difference in the incidence of puncture complications in the use of sheath equal or larger than 8 Fr. (19 cases, 1.2%) and the sheath smaller than 8 Fr. (75 cases, 1.1%). Regarding the age, there was no difference in the frequency of complications between those aged 75 or older (68 cases, 0.7%) and those younger than 75 (190 cases, 0.7%). Although 40% of the puncture complications were treated conservatively, 13% were treated endovascularly and 5% underwent direct surgery.

**Discussion**

In this study, the incidence of puncture site-related complications was 0.73%, which is substantially lower than previously reported 3.1–9.7%.\(^1,2,4,7,8\) Compared with our previous study based on JR-NET1 & 2 data, puncture site-related complications had also very low incidence of 0.63%.\(^6\) As a result of strict management of puncture complications in Japanese endovascular treatment facilities, low incidence of puncture site-related complications is estimated. CAS and extracranial PTA are associated with higher incidence of complications mainly due to intraoperative heparinization, the use of multiple antiplatelet agents, larger diameter sheaths, and peripheral atherosclerosis. There was no difference in puncture complications related with alteplase administration in acute revascularization therapy.

In case of acute revascularization, a 9-Fr guiding catheter with a balloon is often used in Japan. Since a puncture site hemostatic device is applicable only for catheters up to 8 Fr, it was estimated that

---

**Table 2 Sub-analysis of puncture site-related complications frequency**

| Details                                      | Cases  | Puncture site complications (%) | Data unavailable | \( P \)-value |
|----------------------------------------------|--------|---------------------------------|------------------|--------------|
| Acute recanalization therapy tPA (+)         | 1396   | 8 (0.6)                         | 0                | 0.96         |
| tPA (-)                                      | 2492   | 14 (0.6)                        |                  |              |
| Carotid artery stent sheath size <8 Fr      | 1597   | 19 (1.2)                        | 667              | 0.85         |
| ≥8 Fr                                        | 6625   | 75 (1.1)                        |                  |              |
| Age <75 y/o                                  | 26027  | 190 (0.7)                       | 57               | 0.64         |
| ≥75 y/o                                      | 9947   | 68 (0.7)                        |                  |              |
using catheters over 8 Fr would lead to puncture site complications, but it turned to be similar to other groups. There is concern about an increase in complications at the puncture site due to the intravenous administration of alteplase prior to endovascular treatment. In this study, the use of tPA did not lead to the increase in puncture site complications. The results were in line with those in the recent publication.  

Recent reports have shown that hemostasis can be achieved using various hemostatic devices without increasing complication rate. In the carotid stent group, there was no difference in the incidence of puncture site complications between 8 and 6 Fr sheath use, presuming that the hemostatic device was effectively used. In our previous study on the effectiveness of Angio-Seal, it was shown that the occurrence frequency of the puncture site complications is not related to the sheath size.  

It was estimated that the progression of arteriosclerosis increasing with age may cause an increase in puncture-related complications, but this study did not show any increase in complications depending on age.  

The treatment outcome was asymptomatic or transiently symptomatic in 90.5%, but caused disability in 7.0%. Death-related access site complications occurred in six patients (0.016%), but those patients had not only access site, but also other (ischemic and/or hemorrhagic) complications. In this study, it cannot be definitively concluded whether the treatment outcome was affected by puncture site-related complications or not, because some patients had not only puncture site-related, but also other complications. Most puncture site complications resolved after conservative therapy, but in a few cases additional endovascular treatment or open surgery were necessary.  

Looking at the annual trends of retrospectively registered studies in JR-NET1–3, conducted from 2005 to 2012, the same trend was found in occurrence frequency, severity, and cause with the respect to puncture complications. Although there are no innovations and advances in development of hemostasis devices, vascular puncture-related complications have been strictly managed in Japanese endovascular treatment facilities, and thus a low puncture complication rate has been maintained.  

Regarding the limitations, it was a retrospective study based on the registry data, and no description whether the hemostasis was done by the main operator or the assistant was provided. The evaluation criteria for puncture site complications in particular are ambiguous and may be underestimated due to oversight. There was no distinction between using a hemostatic device or manual compression to achieve hemostasis. Regarding puncture site complications, some data may be missing, which may affect statistical analysis.  

**Conclusion**  
The incidence of puncture site vascular complications was 0.73%. These complications resulted in permanent disability in 22 patients (0.06%) and death in six patients (0.017%). CAS, extracranial PTA, and use of antiplatelet drugs were associated with higher incidence of complications. Compared with JR-NET1–3 data were comparable in terms of puncture site complications.  

**Funding Sources**  
This study was supported in part by a Grant-in-Aid (Junkanki-Kaihatsu H24-4-3) from the National Cerebral and Cardiovascular Center, Japan and by Hatazaki Foundation, Kobe, Japan.  

**Acknowledgments**  
"The JR-NET3 Study Group" Co-Principal investigator; Nobuyuki Sakai, Kobe City Medical Center General Hospital, Kobe, Japan, Koji Iihara, Kyushu University, Fukuoka, Japan, Tetsu Satow, National Cerebral and Cardiovascular Center, Saitama, Japan, Investigators; Masayuki Ezura, Sendai Medical Center, Sendai, Japan, Akio Hyodo, Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan, Shigeru Miyachi, Aichi Medical University, Aichi, Japan, Susumu Miyamoto, Kyoto University, Kyoto, Japan, Yoji Nagai, Kobe University, Kobe, Japan, Kunihiro Nishimura, National Cerebral and Cardiovascular Center, Saitama, Japan, Kazunori Toyoda, National Cerebral and Cardiovascular Center, Saita, Japan; Co-investigators; Toshiyuki Fujinaka, Osaka Medical Center, Osaka, Japan, Toshio Higashi, Fukuoka University, Fukuoka, Japan, Masaru Hirohata, Kurume University, Kurume, Japan, Akira Hyodo, Kyoto University, Kyoto, Japan, Hiroto Ishii, Kyushu University, Fukuoka, Japan, Ichiro Nakahara, Fujita Medical University, Aichi, Japan, Chiaki Sakai, Kyushu University, Fukuoka, Japan, Masaru Hirohata, Kurume University, Kurume, Japan, Tetsu Satow, National Cerebral and Cardiovascular Center, Suita, Japan, Kazunori Toyoda, National Cerebral and Cardiovascular Center, Suita, Japan; Co-investigators; Toshiyuki Fujinaka, Osaka Medical Center, Osaka, Japan, Toshio Higashi, Fukuoka University, Fukuoka, Japan, Masaru Hirohata, Kurume University, Kurume, Japan, Akira Hyodo, Kyoto University, Kyoto, Japan, Hiroto Ishii, Kyushu University, Fukuoka, Japan, Ichiro Nakahara, Fujita Medical University, Aichi, Japan, Chiaki Sakai, Hyogo College of Medicine, Nishinomiya, Japan, Kenji Sugiu, Okayama
University, Okayama, Japan, Tomoaki Terada, Showa University Fujigaoka Hospital, Kanagawa, Japan, Shinichi Yoshimura, Hyogo College of Medicine, Nishinomiya, Japan, and Certified Specialist of Japanese Society of Neuroendovascular Therapy. The authors thank Dr. Alexander Zaboronok, Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, for manuscript revision.

Conflicts of Interest Disclosure

We declare no conflicts of interest. All authors who are members of The Japan Neurosurgical Society (JNS) have registered self-reported COI disclosure statement forms online through the website for JNS members.

References

1) Das R, Ahmed K, Athanasiou T, Morgan RA, Belli AM: Arterial closure devices versus manual compression for femoral haemostasis in interventional radiological procedures: a systematic review and meta-analysis. Cardiovasc Intervent Radiol 34: 723–738, 2011
2) Sato M, Matsumaru Y, Sakai N, Yoshimura S, JR-NET study group affiliations: Detailed analysis of puncture site vascular complications in Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2. Neurol Med Chir (Tokyo) 54: 17–22, 2014
3) Upponi SS, Ganeshan AG, Warakaulle DR, Phillips-Hughes J, Boardman P, Uberoi R: Angioseal versus manual compression for haemostasis following peripheral vascular diagnostic and interventional procedures—a randomized controlled trial. Eur J Radiol 61: 332–334, 2007
4) Vaitkus PT: A meta-analysis of percutaneous vascular closure devices after diagnostic catheterization and percutaneous coronary intervention. J Invasive Cardiol 16: 243–246, 2004
5) Veasey RA, Large JK, Silberbauer J, et al.: A randomized controlled trial comparing StarClose and AngioSeal vascular closure devices in a district general hospital—the SCOAST study. Int J Clin Pract 62: 912–918, 2008
6) Sato M, Matsumaru Y, Sakai N, et al.: Usefulness of an access-site hemostasis device in neuroendovascular treatment. Acta Neurochir (Wien) 159: 2331–2335, 2017
7) Koreny M1, Riedmüller E, Nikfardjam M, Siostrzonek P, Müllner M: Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. JAMA 291: 350–357, 2004
8) Stegemann E, Hoffmann R, Marso S, Stegemann B, Marx N, Lauer T: The frequency of vascular complications associated with the use of vascular closure devices varies by indication for cardiac catheterization. Clin Res Cardiol 100: 789–795, 2011
9) Janssen H, Killer-Oberpfalxer M, Lange R: Closure of large bore 9 F arterial puncture sites with the AngioSeal STS device in acute stroke patients after intravenous recombinant tissue plasminogen activator (rt-PA). J Neurointerv Surg 11: 28–30, 2019
10) Goto S, Ohshima T, Ishikawa K, et al. Suitability of a 7-F ExoSeal vascular closure device for femoral artery punctures made by 8-F or 9-F introducer sheaths. J Endovasc Ther 24: 516–520, 2017

Address reprint requests to: Yuji Matsumaru, MD, PhD, Department of neurosurgery, Faculty of Medicine, University of Tsukuba, 2-1-1 Amakubo, Tsukuba, Ibaraki 305-8576, Japan. e-mail: yujimatsumaru@md.tsukuba.ac.jp