maintenance immunosuppression, facilitated the long-term control of rejection, and decreased the incidence of opportunistic infections, resulting in a high rate of patient and graft survival [16]. The combination of rATG and rituximab was an effective induction therapy according to our preliminary data. The number and severity of rejection episodes increased when the liver was not included as part of the graft. An immunosuppression regimen including rATG, rituximab, and steroids may have a protective effect against post-transplant lympho proliferative disease (PTLD) and chronic rejection [17]. Sirolimus is a safe rescue therapy in children with intestinal transplants when tacrolimus is not well tolerated. Renal function and hematologic disorders seem to improve, although other simultaneous strategies could be involved [18]. However, those medications are not commercially available with insurance coverage in Japan. Children after intestinal transplant should be managed with limited immunosuppression.

Preemptive assessments are recommended, even for patients doing well on PN, and for infants and adults with an ultra-short gut or for infants with total intestinal aganglionosis or microvillus inclusion disease, since patients with these findings have very poor survival rates on PN [15].

Early referral and listing are important for successful outcomes. Presently, because of the risks involved as well as financial reasons, transplants are rarely offered to pediatric patients in Japan. However, this treatment will undoubtedly become more common over time as the results of intestinal transplantation continue to improve.

Conclusion

Intestinal transplantation has become the definitive treatment for patients with chronic intestinal failure. Since intestinal transplantation in Japan has yielded satisfactory results, indications for the procedure should be expanded. The national health insurance should cover intestinal transplants to reduce the incidence of PN-related complications. Systems facilitating combined simultaneous liver–intestine and multi-organ transplants should be developed. We continue to work on reforming national health insurance coverage and realizing multi-organ transplantation in Japan.

Acknowledgments This research was partially supported by Health Labor Sciences Research Grant of Ministry of Health, Labor and Welfare, Japan. Japanese intestinal transplant registry is managed by the Japanese Society for Intestinal Transplantation. Also, the authors thank the following institutions for the cooperation in the survey.HBP Surgery and transplantation, Kyoto University: Pediatric Surgery, Tohoku University School of Medicine; Surgery, Keio University Graduate School of Medicine; Pediatric Surgery, Kyusyu University School of Medicine; Pediatric Surgery, Osaka University Graduate School of Medicine.

References

1. Goulet O, Ruemmele F (2006) Causes and management of intestinal failure in children. Gastroenterology 130(2 Suppl 1): S16–S28
2. DeLegge M, Alsolaiman MM, Barbour E et al (2007) Short bowel syndrome: parenteral nutrition versus intestinal transplantation. Where are we today? Dig Dis Sci 52(4):876–892
3. Wales PW, de Silva N, Kim J et al (2004) Neonatal short bowel syndrome: population-based estimates of incidence and mortality rates. J Pediatr Surg 39(5):690–695
4. Maroulis J, Kalfarentzos F (2000) Complications of parenteral nutrition at the end of the century. Clin Nutr 19(5):295–304
5. Cole CR, Frem JC, Schmotzer B et al (2010) The rate of bloodstream infection is high in infants with short bowel syndrome: relationship with small bowel bacterial overgrowth, enteral feeding, and inflammatory and immune responses. J Pediatr 156(6):941–947 947. e1
6. van Ommen CH, Tabbers MM (2010) Catheter-related thrombosis in children with intestinal failure and long-term parenteral nutrition: how to treat and to prevent? Thromb Res 126(6):465–470
7. Gura KM, Lee S, Valim C et al (2008) Safety and efficacy of a fish-oil-based fat emulsion in the treatment of parenteral nutrition-associated liver disease. Pediatrics 121(3):e678–e686
8. Cober MP, Teitelbaum DH (2010) Prevention of parenteral nutrition-associated liver disease: lipid minimization. Curr Opin Organ Transpl 15(3):330–333
9. Magee JC, Krishnan SM, Benfield MR et al (2008) Pediatric transplantation in the US, 1997–2006. Am J Transpl 8(4 Pt 2):935–945
10. Grant D (2011) Small bowel transplant Registry. In: 12th International Small Bowel Transplant Symposium. Washington DC
11. Rodrigues AF, van Mourik ID, Sharif K et al (2006) Management of end-stage central venous access in children referred for possible small bowel transplantation. J Pediatr Gastroenterol Nutr 42(4):427–433
12. Sudan D (2010) Long-term outcomes and quality of life after intestinal transplantation. Curr Opin Organ Transpl 15(3):357–360
13. Ueno TW, Hoshino M, Sakamoto K, Furukawa S, Fukuzawa H, M. (2013) A national survey of patients with intestinal motility disorder who are potential candidate for intestinal transplantation in Japan. Transpl Proc 45(5):2029–2031
14. Tzakis AG, Kato T, Levi DM et al (2005) 100 multivisceral transplants at a single center. Ann Surg 242(4):480–490 discussion 491–3
15. Grant D, Abu-Elmagd K, Reyes J et al (2005) 2003 report of the intestinal transplant registry: a new era has dawned. Ann Surg 241(4):607–613
16. Reyes J, Mazariegos GV, Abu-Elmagd K et al (2005) Intestinal transplantation under tacrolimus monotherapy after perioperative lymphoid depletion with rabbit anti-thymocyte globulin (thymoglobulin). Am J Transpl 5(6):1430–1436
17. Vianna RM, Mangus RS, Fridell JA et al (2008) Induction immunosuppression with thymoglobulin and rituximab in intestinal and multivisceral transplantation. Transplantation 85(9): 1290–1293
18. Andres AM, Lopez Santamaria M, Ramos E et al (2010) The use of sirolimus as a rescue therapy in pediatric intestinal transplant recipients. Pediatr Transpl 14(7):931–935

Ann Surg Oncol (2014) 21:1391–1397
DOI 10.1245/s10434-013-3405-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – HEAD AND NECK ONCOLOGY

Computed Tomography (CT) Venography Using a Multidetector CT Prior to the Percutaneous External Jugular Vein Approach for an Implantable Venous-Access Port

Kazuya Kato, MD[1], Masahiko Taniguchi, MD[2], Yoshiaki Iwasaki, MD[3], Keita Sasahara, RT[1], Atsushi Nagase, MD[4], Kazuhiko Onodera, MD[5], Minoru Matsuda, MD[6], Mineko Higuchi, RN[1], Yuko Kobashi, MD[7], and Hiroyuki Furukawa, MD[2]

[1]Department of Surgery, Pippu Clinic, Kamikawa-gun, Hokkaido, Japan; [2]Department of Surgery, Asahikawa Medical University, Asahikawa, Japan; [3]Department of Internal Medicine, Okayama University, Okayama, Okayama, Japan; [4]Department of Surgery, Asahikawa Medical Center, Asahikawa, Japan; [5]Department of Surgery, Hokuyu Hospital, Sapporo, Japan; [6]Department of Surgery, Nihon University, Tokyo, Japan; [7]Department of Radiology, Jikei University, Tokyo, Japan

ABSTRACT

Background and Purpose. The objective of this study was to determine the success rate and complications of using the percutaneous approach of the external jugular vein (EJV) for placement of a totally implantable venous-access port (TIVAP) with a preoperative estimate of the detailed anatomical orientation of the cervical venous plexus using computed tomography venography (CT-V).

Methods. A prospective cohort study of 45 patients in whom placement of a TIVAP was attempted via the right EJV was conducted. The preoperative anatomical estimation of the cervical venous plexus was performed with CT-V using a Multidetector Helical 16-section CT. The angulation between the right EJV and the right subclavian vein, anterior jugular vein, transverse cervical vein, and suprascapular vein was estimated.

Results. CT-V success was achieved in 45 of 45 patients (100 %). A plexus of veins under the clavicle was most commonly responsible for the insertion of the central venous catheter. The EJV approach resulted in a successful cannulation rate of 93 %. No initial complications of pneumothorax or carotid artery puncture occurred during insertion procedures. Late complications occurred in three patients. These included one port erosion (2 %), one catheter occlusion (2 %), and one wound hematoma (2 %). Catheter-related infections were observed in one patient (2 %).

Conclusions. The percutaneous EJV approach with CT-V guidance is an optional method for patients with multiple central venous cannulations, those in hemodialysis, or those with long catheter indwelling periods.

Central venous catheters (CVCs) and totally implantable venous-access ports (TIVAPs) are used for total parenteral nutrition (TPN), medication administration, chemotherapy, and hemodynamic monitoring.[1] The preferred access approach for CVC placement is the right subclavian vein (SCV) or the right internal jugular vein (IJV). This technique carries a risk of complications, including pneumothorax, hemothorax, and arterial puncture, which can cause significant morbidity.[2–6] Although the left IJV and right SCV have been used for secondary access, several studies suggest that both the SCV and the IJV should be avoided because of a high incidence of procedural complications, as well as central stenosis and thrombosis. The occurrence of these complications is increased in patients undergoing hemodialysis and in those with a history of multiple central venous catheterizations.[5–8] Before using the SCV, access via the external jugular veins (EJVs) should be attempted.[4,9,10] The EJV cut-down approach has to be considered a valid, safe, and suitable alternative when the cephalic vein is not feasible.[11,12] EJV catheterization as a CVC placement route is commonly believed to be difficult because of its anatomical problems.[13] Variations at the

First Received: 12 August 2013;
Published Online: 4 December 2013

K. Kato, MD
e-mail: pippuclinickato@gold.ocn.ne.jp

terminal point and angulation of the EJV as it enters the SCV contribute to a high failure rate.[14] Venography performed from multiple access sites may be required to identify a suitable vein for central access. The EJV approach without venography resulted in a successful cannulation rate of 81 % in our previous study. In this study, we describe our clinical experience with percutaneous venous access via the EJV for TIVAP placement with preoperative anatomical estimation through computed tomography (CT) venography (CT-V) using a multidetector helical 16-section CT (MDCT).

PATIENTS AND METHODS

This study was approved by our hospital's Institutional Review Board. All patients referred to us for TIVAP placement through the right IJV underwent clinical and ultrasound examinations of the right side of the neck. If there were obstacles to the placement of a TIVAP through the right IJV, such as IJV occlusion or skin infection overlying the right IJV, a preoperative CT-V was planned before the TIVAP placement. This was a prospective cohort study of consecutively treated adults (range 74–94 years of age) who underwent attempts at TIVAP placement via EJV while receiving care in our hospital. We conducted a prospective observational study of 45 patients over a 20-month period from September 2011 through March 2013. Women accounted for 56 % ($n = 25$) of the study population, with a mean age of 76 years (range 55–94 years). Mean age of the male participants was 79 years (range 75–89 years). The 32 patients had a history of CVC insertion through the right IJV, both IJVs, or SCVs, ranging from one to three catheterizations with mean of 1.6 catheterizations. Two patients had a history of non-tunneled catheters for temporary hemodialysis. The indication for TIVAP placement was TPN in 31 patients (69 %), chemotherapy for solid and hematologic malignancies in four patients (8 %), and long-term antibiotic administration or blood transfusion in three patients (6 %). Patients with impaired renal function were excluded from this study. The choice of insertion route was based on the angulation between the EJV and the cervical venous plexus on CT-V. The catheter course and tip location were verified by a radiograph on the 1st, 7th, and 30th day, as well as at 6 and 12 months after insertion. The data included the inability to thread the catheter centrally, eventual CVC location, CVC adjustments needed, initial complications (pneumothorax and carotid artery puncture), late complications including catheter occlusion, catheter transection, catheter migration, symptomatic venous thrombosis, wound hematoma, port erosion, operating time, dwell time (time from insertion to removal), and catheter-related infection rate. A major procedural complication was one requiring active intervention, and a minor procedural complication required only conservative therapy. Premature TIVAP removal was defined as removal for causes other than patient demise, termination of therapy, or termination of study. Symptomatic venous thrombosis was clinically assessed according to whether symptoms such as facial edema and right-arm swelling with or without pain developed after the EJV catheterization, including the follow-up MDCT and ultrasonography studies. Catheter-related infection included insertion site infection and catheter-related bacteremia. Insertion site infection was defined as infection localized to the catheter exit. Line sepsis is equivalent to catheter-related bacteremia,[4] which was defined as a clinical episode of sepsis in which there was a high index of clinical suspicion that the catheter was the source of the sepsis.

Scanning Parameters

The CT-V was performed with a 16-MDCT scanner (BrightSpeed Elite SD, GE Healthcare, Fairfield, CT, USA). The CT-V of the cervical area involved scanning from the base of the C1 vertebral body to the level of pulmonary hila after a fixed 40-s delay between the onset of the contrast material injection and the start of scanning. A 100 mL volume of non-ionic iodinated contrast material (Iopamiron 300™, Bayer HealthCare, Leverkusen, Germany) was injected into a right antecubital vein at a rate of 3 mL per second using a power injector. The following scanning and reconstruction parameters were used for the multidetector CT venogram acquisition: 1.25-mm collimation; pitch of 1.375; a 1.25-mm reconstruction increment; and a 0.8-s rotation time. A low-dose technique was used, with a tube current of 100–250 mAs and a peak kilovoltage of 120 kVp. The technique values for the multidetector row CT used in this study (120 kVp, 50 mA) were chosen so that the image noise would match that found with the single-section technique (120 kVp, 70 mA). The pitch needed to be varied to account for differences in patient length so that the acquisition could be completed in 30 s. After scout images were acquired, images with the patient in the supine position were obtained. The MDCT scans were acquired from the level of the C1 vertebral body to the level of pulmonary hila with *z*-axis coverage of 32–38 cm and with the patient in a supine position. Standard maximum intensity projection images of the major cervical venous structures were created by the three-dimensional (3D) laboratory. A primary two-dimensional (2D) evaluation technique (axial views, 2D-CT) was applied using multiplanar reformatted (MPR) images and a 3D view. GE Navigator software enabled the simultaneous review of 3D-CT vessels, coronal and sagittal MPR, and axial images.

Image Analysis

Image processing was performed with a workstation (2LCD Workflow, GE, Healthcare for Linux) using a combination of soft-tissue windows (window width 400 HU; window level 40 HU) and bone windows (window width 2,000 HU; window level 0 HU), multiplanar reformats, and 3D problem solving. Data were examined using transverse CT images with the concurrent display of both 2D and 3D reformatted images for measuring the angulation between vessels with a 3D workstation (BrightSpeed Elite SD). The reconstructed images were analyzed for parameters with implications for the CVC placement, including the angle of the EJV at four locations: the angle between the left EJV and the SCV, the angle between the left EJV and the anterior jugular vein (AJV), the angle between the left EJV and the transverse cervical vein (TCV), and the angle between the left EJV and the suprascapular vein (SSV). We examined the data to assess which junction was most responsible for the insertion of a CVC.

Percutaneous Insertion Technique for EJV

The patient was placed in a 20° Trendelenburg position to distend the EJV, and patency was confirmed by ultrasonography. An anesthetic patch was attached to the insertion site of the skin before catheter insertion. The right side of the neck and the upper chest of the patient were prepared with sterile technique. The right EJV was identified by visual inspection and palpation, and then punctured. An EJV puncture was performed under sterile conditions with a 14-gauge introducer needle (over-the-needle Teflon catheter, BD Insyte I.V. Catheter^{TM}, Becton–Dickinson, Infusion Therapy Systems, Inc., Sandy, UT, USA) (Fig. 1a, b). The Seldinger technique was used to access the EJV with dilators and peel-away sheaths for the insertion, which used an 18-gauge polyurethane CVC (Bard Access Port, SlimPort 6F^{TM}, Bard Access system Inc., Salt Lake City, UT, USA) that was 75 cm in length (Fig. 1c). Under fluoroscopic control, the catheter was driven toward the SCV, the innominate vein, and finally the SVC, where the tip of the catheter was positioned. A port was placed in a tight subcutaneous chamber, over the pectoralis fascia, 4 cm under the clavicle (Fig. 1d). In cases where the preoperative CT-V demonstrated a sharp angulation of the EJV to the SCV (EJV–SCV sharp-angle type), an obtuse angulation between the EJV and the AJV (EJV–AJV obtuse-angle type), or an obtuse angulation between the EJV and the TCV or the SSV (EJV–TCV/SSV obtuse-angle type), which might cause difficulties in inserting the catheter or cause the catheter to become kinked or knotted, a guide wire (a 35-cm long, 0.089-cm diameter, flexible angiographic catheter guide wire: angle type, Radifocus guide wire M^{TM}, Terumo, Tokyo, Japan) technique[12] was used under fluoroscopy. In cases where the preoperative CT-V demonstrated an obtuse-angle type EJV–TCV/SSV, which might cause difficulties in inserting the catheter or cause the catheter to thread to the SCV, an ultrasound-guided right femoral vein (FV) cannulation was used.[13,14] Chest radiographs (CXRs) were obtained after the procedure.

RESULTS

A total of 45 patients were enrolled in the study. Successful CT-V was achieved in 45 of 45 patients (100 %) (Fig. 2a, b). There were no complications from the CT-V in any of the 45 patients. Mean angulation between the right EJV and the right SCV was 144° ± 36° in the obtuse-angle cases (88 %) (Fig. 3a) and 72° ± 28° in the EJV–SCV sharp-angle type (12 %) (Fig. 3b). Mean angulation between the EJV and the AJV was 125° ± 12° in the EJV–AJV obtuse-angle type (10 %) and 45° ± 5° in the sharp-angle cases. Mean angulation between the EJV and the TCV or SSV (Fig. 3c) was 133° ± 5° in the EJV–TCV/SSV obtuse-angle type (8 %) and 61° ± 20° in the sharp-angle cases (Fig. 3d). Central venous access via the EJV was obtained in 42 (93 %) of 45 patients. The average number of puncture attempts was 1.45 (range 1–4) and the average procedure time was 13.5 min (range 9–25 min). In ten patients, the preoperative CT-V demonstrated a sharp-angle type EJV–SCV, an obtuse-angle type EJV–AJV, or an obtuse-angle type EJV–TCV/SSV [15] (Table 1). In seven of the patients with an EJV–SCV sharp-angle type (four patients) or an EJV–AJV obtuse-angle type (three patients), TIVAP placement via EJV was obtained using a Radifocus guide wire M^{TM} technique under fluoroscopy after the J-guide wire technique failed. In the three patients with an obtuse-angle type EJV–TCV/SSV, right FV cannulation was used. In the remaining 35 patients, the catheters were inserted via the right EJV without any problem. Successful placement of a TIVAP was accomplished in all patients. The catheter dwell time ranged from 65 to 325.5 days, with a mean dwell time of 255.5 days. There were no significant procedural complications (pneumothorax, expanding hematoma, or carotid artery puncture) during the 43 catheterization attempts. In five patients (12 %), a small amount of subcutaneous bleeding over the EJV was observed. Late complications occurred in three patients. These included one port erosion (2 %), one catheter occlusion (2 %), and one wound hematoma (2 %). Catheter-related infections were observed in one patient (2 %). The catheter-related infection was catheter-related bacteremia, which occurred at 65 catheter days in a patient undergoing chemotherapy who had the catheter removed (Fig. 4). No thrombotic complications were demonstrated.

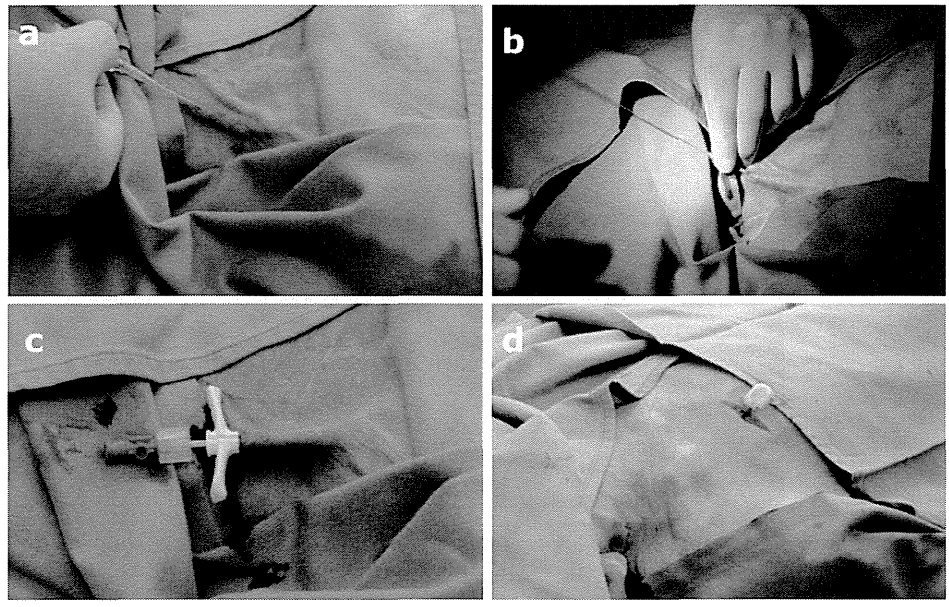

FIG. 1 **a** Puncture of a right EJV was attempted with a 16-gauge over-the-needle Teflon catheter. **b** The J-guide wire was inserted and advanced into the central venous position. **c** The dilator and peel-away sheath were inserted over the wire and then an 18-gauge, 20 cm polyurethane radiopaque catheter was inserted in a smooth, one-step maneuver. **d** A port was placed in a tight subcutaneous chamber, over the pectoralis fascia, 4 cm under the clavicle

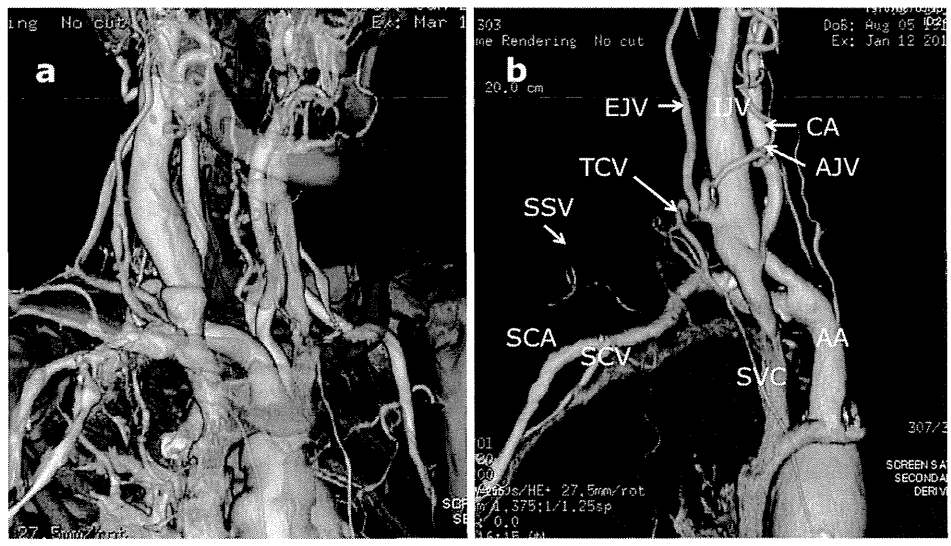

FIG. 2 MDCT venography of the cervical venous plexus: antero-posterior volume-rendered images (**a**, **b**). The CT-V showed a detailed cervical venous plexus and the central venous system. It also clearly revealed individual vascular anatomies around the EJV and SCV junction. *MDCT* multidetector computed tomography, *CT-V* computed tomography venography, *EJV* external jugular vein, *SCV* subclavian vein, *IJV* internal jugular vein, *CA* carotid artery, *AJV* anterior jugular vein, *TCV* transverse cervical vein, *SSV* suprascapular vein, *SCA* subclavian artery, *SVC* superior vena cava, *AA* aortic arch

DISCUSSION

The technique of central venous catheterization via the EJV was reported in 1974.[9] The EJV approach has not been popular because of its low success rate,[13] which is due to further anatomical considerations. Although the EJV cut-down approach for central venous access is well described in the literature,[11] there are few data available that specifically address the potential utilization of EJV for TIVAP placement. In this study, the success rate of the EJV puncture approach was 93 %, whereas the success of the CV cut-down approach has been reported as 93 %.[12] The

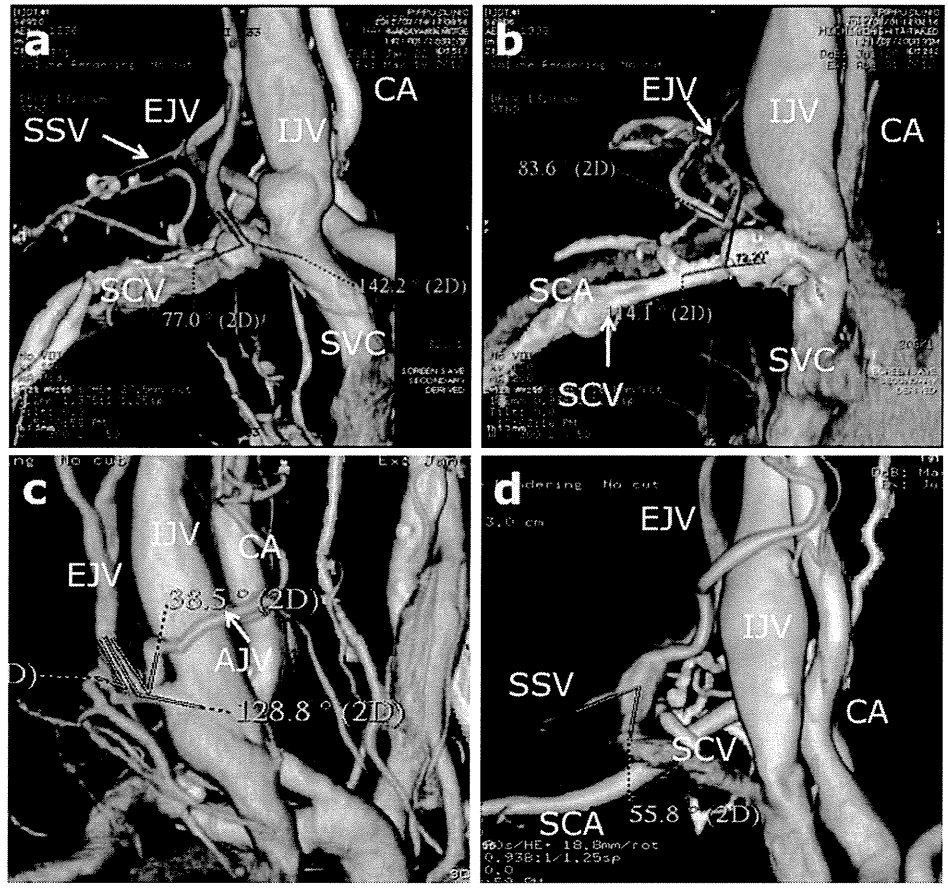

FIG. 3 MDCT venography: (**a**, **b**) anteroposterior volume-rendered images. The CT-V showed the angle between the right EJV and the right SCV. Mean angulation between the EJV and the SCV measured 144° ± 36° in the obtuse-angle cases (**a**), and 72° ± 28° in the sharp-angle cases (**b**). Mean angulation between the EJV and the AJV measured 133° ± 5° in the obtuse-angle cases (**c**). Mean angulation between the EJV and the SSV measured 61° ± 20° in the sharp-angle cases (**d**). *MDCT* multidetector computed tomography, *CT-V* computed tomography venography, *EJV* external jugular vein, *SCV* subclavian vein, *AJV* anterior jugular vein, *SSV* suprascapular vein

TABLE 1 Angulation between the right EJV and SCV or AJV or TCV/SSV

Angulation type	SCV	AJV	TCV/SSV
Sharp	70 ± 29 (14)	45 ± 13 (95)	62 ± 26 (92)
Obtuse	140 ± 30 (86)	132 ± 15 (5)	137 ± 8 (8)

Data are presented as mean angulation (degree) (%)

EJV external jugular vein, *SCV* subclavian vein, *AJV* anterior jugular vein, *TCV* transverse cervical vein, *SSV* suprascapular vein

benefits inherent in the use of the EJV include its large size and a greater ability to accommodate large or multilumen catheters more easily than many peripheral insertion sites, the superficial location, the ability to visualize the EJV without imaging technology, and the ease of access in reaching the SVC. The angulation between the EJV and the TCV/SSV was responsible for insertion success in our preliminary study. Catheterization from the EJV requires a detailed anatomical orientation of these vessels, including the central vascular system, before catheter insertion. Three-dimensional CT-V using MDCT clearly revealed individual vascular anomalies around the EJV and the SCV junction and could play an important role in safe cannulation. When compared with the IJV or SCV sites, the EJV site offers a small risk of bleeding, puncture of the carotid artery, or pneumothorax in frail, elderly patients.

The development of contrast-induced nephropathy (CIN) is related to the number of risk factors present, with the most important being renal insufficiency, diabetes mellitus, and volume of contrast agent used. Most studies show that, within a class, higher volumes (>100 mL) of iodinated contrast medium are associated with a higher risk for CIN.[16] There is evidence that low-osmolar contrast media are less nephrotoxic than high-osmolar contrast media in patients at increased risk for CIN.[16] We recommended that the dose not exceed 100 mL of non-ionic iodinated low-osmolar contrast agents in the CT-V.[17]

Our results demonstrate that percutaneous EJV cannulation is safe for central venous access, with a high success rate compared with other sites. Superficial hematoma was the only problem found with the EJV route in our study, and it was most often observed in the failed attempts. The site for percutaneously inserted catheters is determined by multiple factors, including the clinical status of the patient, the purpose of central access, the anticipated length of time it will be needed, and physician experience.[11] The most important advantage is the absence of major complications.

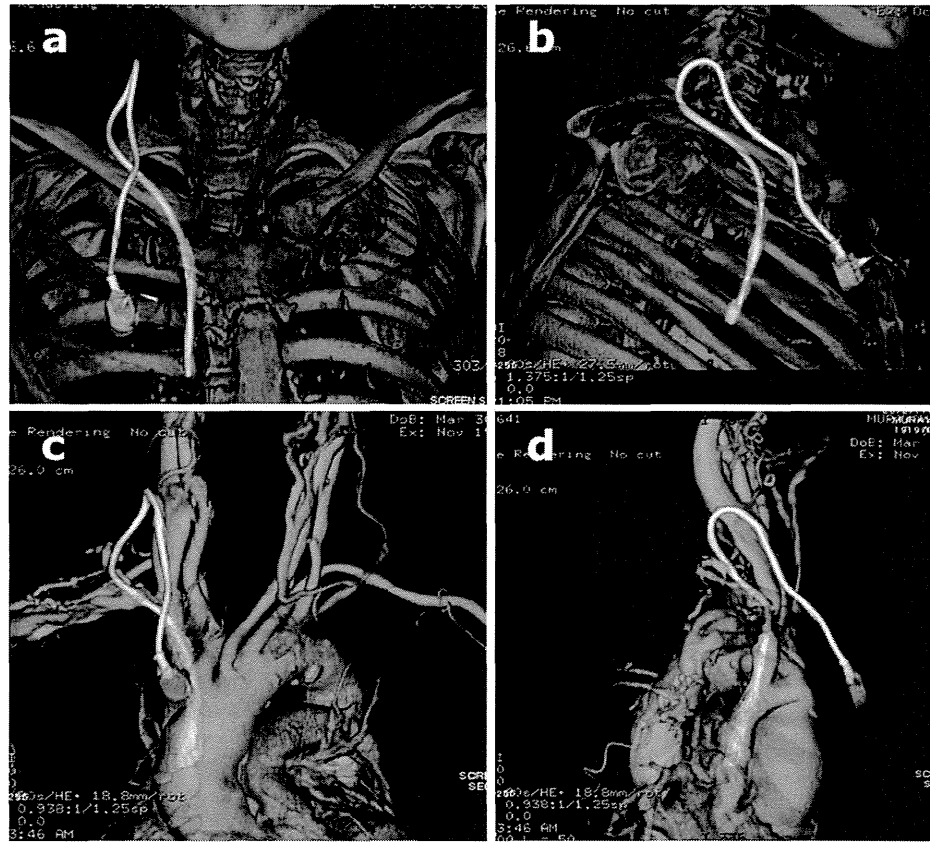

FIG. 4 Follow-up MDCT: anteroposterior (**a**) and lateral (**b**) volume-rendered images. Follow-up MDCT venography: anteroposterior (**c**) and lateral (**d**) volume-rendered images. The MDCT showed the appropriate TIVAP position and the catheter position. *MDCT* multidetector computed tomography, *TIVAP* totally implantable venous-access port

In regard to patient safety, it is worth nothing that in the relatively recent past, the use of peripherally inserted central catheters has obviated some of the risks involved with more central access sites. Therefore, central venous access via the EJV for the placement of TIVAP seems to be an option to consider for vascular access in patients, given our findings of a high success rate and a low complication rate.[18]

The present study has some limitations. Our study was preliminary in its prospective nature and the lack of a control group. The number of reported cases is relatively small, which implies the need for a study involving a large patient population that would permit a more precise assessment. Further studies are needed to determine how these advances in central access compare with the safety profile of the EJV technique with CT-V for the placement of a TIVAP.

CONFLICT OF INTEREST None of authors have identified any conflicts of interest.

REFERENCES

1. Gorman RC, Buzby GP. Difficult access problems. *Surg Oncol Clin North Am.* 1995;4:453–472.
2. Bermard RW, Stahl WM. Subclavian vein catheterizations: a prospective study. I: non-infectious complications. *Ann Surg.* 1971;173:184–190.
3. Mansfield PF, Hohn DC, Forange BD, Gregurich MA, Ota DM. Complications and failures of subclavian-vein catheterization. *N Engl J Med.* 1994;29:1735–1738.
4. Trerotola SO. You are asked to place a dialysis access catheter in a patient. What is your preferred access site, and why? *J Vasc Interv Radiol.* 1997;8:75–76.
5. Macdonald S, Watt AJB, McNally D, Edwards RD, Moss JG. Comparison of technical success and outcome of tunneled catheters inserted via the jugular and subclavian approach. *J Vasc Interv Radiol.* 2000;11:225–231.
6. Schillinger F, Schillinger D, Montagnac R, Milcent T. Post catheterization vein stenosis in haemodialysis: comparative angiographic study of 50 subclavian and 50 internal jugular access. *Nephrol Dial Transplant.* 1991;6:722–7124.
7. Moss AH, McLaughlin MM, Lempert KD, Holley JL. Use of a silicone catheter with a Dacron cuff for dialysis short-term vascular access. *Am J Kidney Dis.* 1988;12;492–489.
8. Trerotola SO, Kuhn-Fulton J, Johnson MS, Shah H, Ambrosius WT, Kneebone PH. Tunneled infusion catheters: increased incidence of symptomatic venous thrombosis after subclavian versus internal jugular venous access. *Radiology.* 2000;217:89–93.
9. Susan NW: Unconventional venous access. *Tech Vas Interv Radiol.* 2001;5:114–120.
10. Cho SK, Shin SW, Do YS, Park KB, Choo SW, Choo IW. Use of the right external jugular vein as the preferred access site when the right internal jugular vein is not usable. *J Vasc Interv Radiol.* 2006;17:823–829.

11. Povoski SP. External jugular vein cutdown approach for chronic indwelling central venous access in cancer patients: a potentially useful alternative. *World J Surg Oncol.* 2004;2:7–11.
12. Di Carlo I, Barbagallo F, Toro A, Sofia M, Lombard R, Cordio S. External jugular vein cutdown approach, as a useful alternative, support the choice of cephalic vein for totally implantable access device placement. *Ann Surg Oncol.* 2005;12:570–573.
13. Malatinsky J, Kadlic T, Majek M, Samel M. Misplacement and loop formation of central venous catheters. *Acta Anaesth Scand.* 1976;20:237–247.
14. Blitt CD, Wright WA, Petty WC, Webster TA. Central venous catheterization via the external jugular vein. *JAMA.* 1974;229:817–818.
15. Deshpande KS, Hatem C, Ulrich HL, et al. The incidence of infectious complications of central venous catherters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Critical Care Med.* 2005;33:13–22.
16. Lenhard DC, Pietsch H, Sieber MA, Ernst R, Lengsfeld P, Ellinghaus P, Jost G. The osmolality of nonionic, iodinated contrast agents as an important factor for renal safety. *Invest Radiol.* 2012;47:503–510.
17. Davidson C, Stacul F, McCullough PA, Tumlin J, Adam A, Lameire N, et al. Contrast medium use. *Am J Cardiol.* 2006;98:42K–58K.
18. Heye S, Maleux G, Claes K, Kuypers D, Oyen R. Stenosis detection in native hemodialysis fistulas with MDCT angiography. *Am J Roentgenol.* 2009;192;1079–1084.
19. Gordon AC, Saliken JC, Johns D, Owen R, Gray RR. US-guided puncture of the internal jugular vein: complications and anatomic considerations. *J Vasc Interv Radiol.* 1998;9:333–338.
20. Shih YC, Chien HL, Hao MC, Huan MH, Jyh CY. A safe and effective method to implantable access port in patients with synchronous bilateral mastectomies: modified femoral vein approach. *J Surg Oncol.* 2008;98:197–199.

Journal of Investigative Surgery, 27, 176–182, 2014

ISSN: 0894-1939 print / 1521-0553 online
DOI: 10.3109/08941939.2013.865818

informa
healthcare

NEW METHODOLOGIES

Central Venous Access via External Jugular Vein with CT-Venography Using a Multidetector Helical 16-Section CT

Kazuya Kato, MD, PhD,[1] Masahiko Taniguchi, MD, PhD,[2] Yoshiaki Iwasaki, MD, PhD,[3] Keita Sasahara, RT,[1] Atsushi Nagase, MD,[4] Kazuhiko Onodera, MD, PhD,[5] Minoru Matsuda, MD, PhD,[6] Mineko Higuchi, RN,[1] Miki Nakano, MT,[1] Yuko Kobashi, MD, PhD,[7] Hiroyuki Furukawa, MD, PhD[2]

[1] *Department of Surgery, Pippu Clinic, Pippu, Town Kamikawa-Gun, Hokkaido, Japan,* [2] *Department of Surgery, Asahikawa Medical University, Midorigaoka, Asahikawa, Japan,* [3] *Department of Internal Medicine, Okayama University, Okayama City, Okayama, Japan,* [4] *Department of Surgery, Asahikawa Medical Center, Asahikawa, Japan,* [5] *Department of Surgery, Hokuyu Hospital, Sapporo, Japan,* [6] *Department of Surgery, Nihon University, Chiyoda-ku Tokyo, Japan,* [7] *Department of Radiology, Jikei University, Nishishinbashi, Minato-ku, Tokyo, Japan*

ABSTRACT

Objective: To determine the success rate and complications of using the external jugular vein (EJV) for central venous access with a preoperative estimate of the detailed anatomical orientation of the cervical venous plexus using computed tomography venography (CT-V). *Design:* Prospective, observational human study. *Setting:* Surgical intensive care unit. *Patients:* Fifty-two patients who were undergoing EJV cannulations with CT-V using a Multidetector Helical 16-section CT (MDCT). *Intervention:* The preoperative anatomical estimation of the cervical venous plexus was performed with CT-V using an MDCT. In particular, the angulation between the EJV and the right subclavian vein (SCV) was measured. The anatomical abnormalities and the angulation between the EJV and the anterior jugular vein (AJV), transverse cervical vein (TCV), and suprascapular vein (SSV) were estimated. *Measurements and Main Results:* The success of CT-V was achieved in 52 of 52 patients (100%). The mean angulation between the right EJV and the right SCV was 144 ± 36 degrees in the obtuse-angle cases (88%) and 72 ± 28 degrees in the sharp-angle cases (12%). A plexus of veins under the clavicle was most commonly responsible for insertion of the central venous catheter (CVC). The EJV approach resulted in a 93% rate of successful cannulations. No complications of pneumothorax or carotid artery puncture occurred during insertion procedures. *Conclusions*: The EJV route is associated with comparable technical success and lower major procedural complication. The EJV approach with CT-V guidance is an option as the initial method when central venous cannulation must be performed under suboptimal conditions.

Keywords: external jugular vein (EJV); catheterization; central venous access; cervical venous plexus; multidetector helical 16-section computed tomography (MDCT); computed tomography venography (CT-V)

INTRODUCTION

Central venous access plays an important role in modern medical care. Central venous catheters (CVCs) are used for total parental nutrition, medication administration, chemotherapy, and hemodynamic monitoring [1]. The preferred access approach for CVC placement is the right subclavian vein (SCV) or the right internal jugular vein (IJV) [2, 3]. The percutaneous Seldinger method for catheter insertion into the SCV has been widely accepted, because of the ease of insertion when initially successful. This technique carries the risk of complications, including pneumothorax, hemothorax, and arterial puncture, that can cause significant morbidity [2, 4–6]. The right IJV approach should be considered as the primary access site for all patients [2, 7]. When the right IJV is not available for CVC placement, the second access site remains

Received 10 September 2013; accepted 11 November 2013.

Address correspondence to Kazuya Kato, MD, PhD, Department of Surgery, Pippu Clinic, 2-10, 1 cyome Nakamachi, Pippu Town Kamikawa-gun, Hokkaido 078-0343, Japan. E-mail: pippuclinickato@gold.ocn.ne.jp

variable. Although the left IJV and both SCVs have been used for secondary access, several studies suggest that both the SCV and the IJV should be avoided because of a high incidence of procedural complications as well as central stenosis and thrombosis [4–6, 8]. These complications are increased in patients undergoing hemodialysis and in those with a history of multiple central venous catheterizations [4, 8].

The external jugular vein (EJV) approach for CVC placement has been reported [9, 10]. One reason to use the right EJV is its relatively straightforward course and short length, similar to the right IJV. A second reason is that the EJV is easily accessible, given its superficial location on the neck [11]. EJV catheterization as a CVC placement route is commonly believed to be difficult because of its anatomical problems. Variations at the terminal point and angulation of the EJV as it enters into SCV contribute to a high failure rate [12]. Of anatomic importance to catheterization is the fact that the EJV forms an acute angle at its insertion into the SCV, which may explain the higher rate of malpositioned catheters [13]. Venography performed from multiple access sites may be required to identify a suitable vein for central access.

Here, we describe our clinical experience with percutaneous venous access via the EJV with preoperative anatomical estimation through computed tomography venography (CT-V) using a multidetector helical 16-section CT (MDCT). We describe procedural techniques that improve the success rate in patients with more difficult venous access.

MATERIALS AND METHODS

This study was approved by our hospital's institutional review board, and a waiver of consent was granted because EJV central venous access was judged one of several routine access technique. This was a prospective cohort study of consecutively treated adults (76–91 years of range) who underwent EJV central venous access attempts while receiving care in our hospital. We conducted a prospective observational study over an 18-month period from September 2011 through March 2013 of 52 patients. Women accounted for 53% ($n = 27$) of the study population, with a mean age of 82 years (range, 76–91 years). The mean age of the male participants was 78 years (range 74–88 years). The indication for CVC placement: 41 patients (78%) were for parenteral nutrition (TPN), 6 patients (12%) were for chemotherapy for solid and hematologic malignancies, and 5 patients (10%) were for long-term antibiotic administration. Fifty-two patients underwent CT-V guided CVC placement, for which informed consent was obtained. The catheter course and tip location were routinely verified by a radiograph on the 1st and 7th day after insertion. The data included inability to thread the catheter centrally, eventual CVC location, CVC adjustments needed, initial and late complications, operating time, dwell time, and catheter-related infection rate. These data, including follow up data catheter removal, were complete for all patients within our institution. These data were recorded on a uniform data sheet by a stuff surgeon.

Scanning Parameters

The CT-V was performed with a 16-MDCT scanner (BrightSpeed Elite SD, GE Healthcare). The CT-V of the cervical area involved scanning from the base of the C1 vertebral body to the level of pulmonary hila after a fixed 40-s delay between the onset of the contrast material injection and the start of scanning. A 100-mL volume of nonionic iodinated contrast material (Iopamiron 300^{TM}, Bayer HealthCare, Leverkusen, Germany) was injected into a right antecubital vein at a rate of 3 mL/s using a power injector. The following scanning and reconstruction parameters were used for the multidectector CT venogram acquisitions: a 1.25-mm collimation, pitch of 1.375, a 1.25-mm reconstruction increment, and a 0.8-s rotation time. A low-dose technique was used, with a tube current of 100–250 mAs and a peak kilovoltage of 120 kVp. The technique values for the multi-detector row CT used in this study (120 kVp, 50 mA) were chosen so that the image noise would match that found with the single-section technique (120 kVp, 70 mA). The pitch needed to be varied to account for differences in patient length so that the acquisition could be completed in 30 s. All of the CT-V examinations were performed under the direct supervision of a radiologist with the ability to immediately interpret the images to ensure optimum image quality. After scout images were acquired, images with the patient in the supine position were obtained. The MDCT scans were acquired from the level of the C1 vertebral body to the level of pulmonary hila with a *z*-axis coverage of 32–38 cm and with the patient in a supine position. Standard maximum intensity projection images of the major cervical venous structures were created by the three-dimensional (3D) laboratory. A primary two-dimensional (2D) evaluation technique (axial views, 2D-CT) was applied using multiplanar reformatted (MPR) images and a 3D view. The GE Navigator software enabled the simultaneous review of 3D-CT vessels, coronal and sagittal MPR, and axial images.

Image Analysis

Image processing was performed with a workstation (2LCD Workflow, GE, Healthcare for Linux) using a combination of soft-tissue windows (window width, 400HU; window level, 40 HU) and bone windows (window width, 2,000 HU; window level, 0 HU), multiplanar reformations, and 3D problem solving. The

data were examined using transverse CT images with the concurrent display of both 2D and 3D reformed images for measuring the angulation between vessels with a 3D-workstation (BrightSpeed Elite SD). The reconstructed images were analyzed for parameters with implications for the CVC placement including the angle of the EJV at four locations: the angle between the left EJV and the SCV, the angle between the left EJV and the anterior jugular vein (AJV), the angle between the left EJV and the transverse cervical vein (TCV), and the angle between the left EJV and the suprascapular vein (SSV). We examined the data to assess which junction was most responsible for the insertion of CVC. The procedures were performed by a staff interventional radiologist.

Insertion Technique for External Jugular Vein

The patient was placed in a 20-degree Trendelenburg position to distend the EJV, and puncture site and patency were confirmed by ultrasonography. The right side of the neck and the upper chest of the patient were prepared with sterile technique. An anesthetic patch was attached to the insertion site of the skin before catheter insertion. The right EJV was identified by visual inspection and palpation and then punctured. An EJV puncture was performed under sterile conditions with a 14-gauge introducing needle (over-the-needle Teflon catheter, BD Insyte I.V. Catheter™, Becton Dickinson, infusion Therapy Sysems Inc., Sandy, Utah, USA). The Seldinger technique was used to access the EJV with a 16-gauge polyurethane central venous catheter (Argyle Medicut Catheter™, Tyco Healthcare, Tokyo, Japan), which is 30-cm in length. In cases where the preoperative CT-V demonstrated a sharp angulation of the EJV to the SCV (EJV-SCV sharp-angle type), or a obtuse angulation between the EJV and the AJV (EJV-AJV obtuse-angle type) or a obtuse angulation between the EJV and the TCV or the SSV (EJV-TCV/SSV obtuse-angle type), which might cause difficulties in withdrawing the catheter or cause the catheter to become kinked or knotted, a guide wire (a 35 cm long, 0.089-cm diameter, flexible angiographic catheter guide wire: angle type, Radifocus guide wire M™, TERUMO, Tokyo, Japan) technique [14] was used under fluoroscopy. In cases where the preoperative CT-V demonstrated the EJV-TCV/SSV obtuse-angle type, an ultrasound-guided right femoral vein (FV) cannulation [15] was used. Chest radiographs (CXRs) were obtained after the procedure. Manipulation of the CVC was made as necessary for acceptable placement. The procedures were performed by a staff surgeon.

RESULTS

A total 52 patients were enrolled over the study. The success of CT-V was achieved in 52 of 52 patients (100%) (Figures 1a and b). There were no complications from the CT-V in any of the 52 patients. The mean angulation between the right EJV and the right SCV measured 144 ± 36 degrees in the obtuse-angle cases (88%) (Figure 1c) and 72 ± 28 degrees in the EJV–SCV sharp-angle type (12%) (Figure 1d). The mean angulation between the EJV and the AJV measured 121 ± 10 degrees in the EJV–AJV obtuse-angle type (6%) (Figure 2a) and 43 ± 8 degrees in the sharp-angle cases (94%) (Figure 2b). The mean angulation between the EJV and the TCV or SSV measured 135 ± 4 degrees in the EJV–TCV/SSV obtuse-angle type (6%) (Figure 2c) and 63 ± 22 degrees in the sharp-angle cases (94%) (Figure 2d) (Table 1). Central venous access via the EJV was obtained in 50 (93%) of 52 patients. Fully completed data sheet were obtained from 50 patients. The average of number of puncture attempts was 1.12 (range, 1–3). The average procedure time was 13 min (range, 7–21 min).

TABLE 1 Angulation between the right EJV and SCV or AJV or TCV/SSV

Angulation type	SCV	AJV	TCV/SSV
Sharp	72 ± 28 (12)	43 ± 8 (94)	63 ± 22 (94)
Obtuse	144 ± 36 (88)	122 ± 10 (6)	135 ± 4 (6)

Note. Data are mean angulation (degree), with percentage in parenthesis.
EJV, external jugular vein; SCV, subclavian vein; AJV, anterior jugular vein; TCV, transverse cervical vein; SSV, suprascapular vein.

In eight patients (15%) where the preoperative CT-V demonstrated an EJV–SCV sharp-angle type, or an EJV–AJV obtuse-angle type or an EJV–TCV/SSV obtuse-angle type, a guide wire technique was used under fluoroscopy [10]. In six patients of EJV-SCV sharp-angle type (4 patients) and EJV–AJV obtuse-angle type (2 patients), CVC placement via EJV was obtained using a guide wire technique under fluoroscopy. In two patients (4%) of EJV–TCV/SSV obtuse-angle type, the right FV cannulations were used after the EJV cannulations have failed. In the remaining 44 patients, the catheter was inserted via the right EJV without any problem. Catheter-tip location on initial CXR was in the upper right atrium (RA) in 2 patients (4%). Fluoroscopy was used to help manipulate the central line for acceptable catheter placement. In one patient, the CT-V could not identify the left IJV, EJV, or the right EJV (Figure 3a). The Doppler color ultrasound demonstrated significantly turbulent flow with a decreased flow velocity in the left IJV (Figures 3b and c). Central venous access via the right EJV was obtained in this patient without any problem.

There were no significant procedural complications (pneumothorax, expanding hematoma, or carotid artery puncture) during the 50 catheterization attempts.

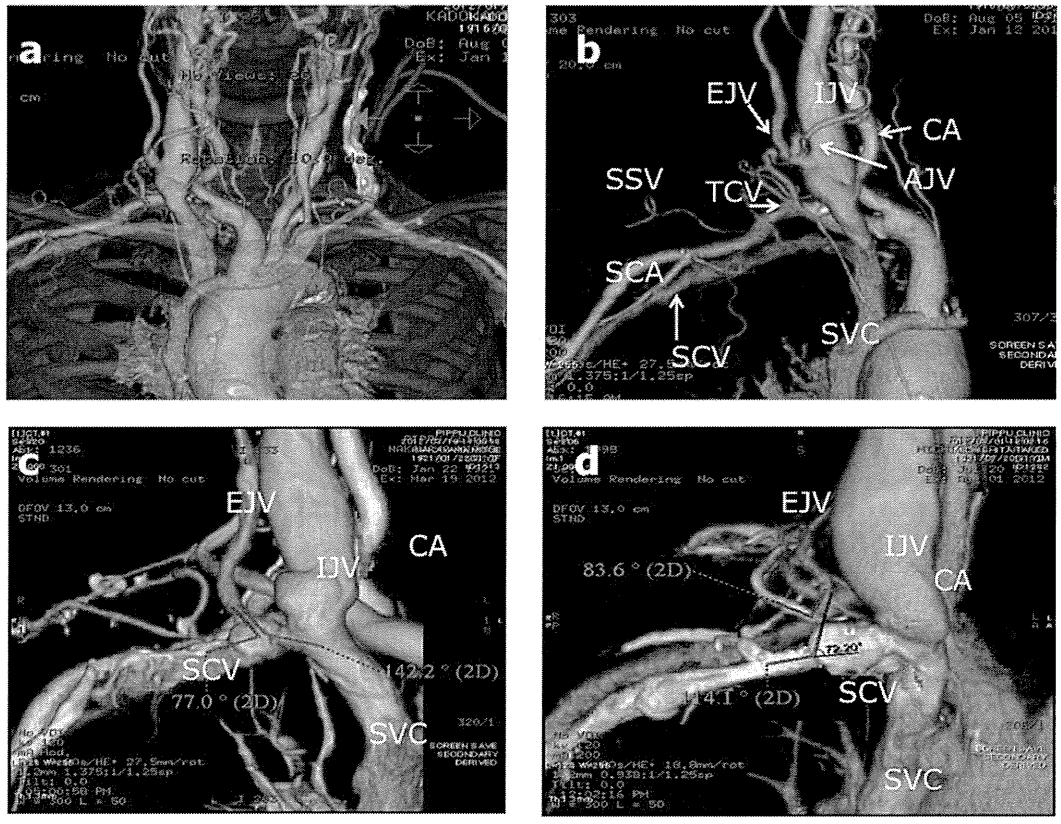

FIGURE 1 (a and b) MDCT venography of the cervical venous plexus: anteroposterior (AP) and lateral volume-rendered (VR) images. The CT-V showed a detailed cervical venous plexus and the central venous system. The CT-V clearly revealed individual vascular anatomies around the EJV and SCV junction. EJV, external jugular vein; IJV, internal jugular vein; CA, carotid artery; AJV, anterior jugular vein; TCV, transverse cervical vein; SSV, suprascapular vein; SCA, subclavian artery; SCV, subclavian vein; SVC superior vena cava; AA, aortic arch. The CT-V showed the angle between the left EJV and the SCV. The mean angulation between the right EJV and the right SCV measured 144 ± 36 degrees in the obtuse-angle cases (c) and 72 ± 28 degrees in the sharp-angle cases (d).

In three patients (6%), the small amount of subcutaneous oozing of the blood over the EJV was observed. The catheter dwell time ranged from 14 to 70 days, with a mean dwell time of 35.2 days. Catheter-related infections were observed in 2 patients (4%). No thrombotic complications were demonstrated on the clinical examination, follow-up MDCT study or ultrasonography in 50 cases during the study.

DISCUSSION

Conventional access sites include the IJV and the SCV. The former should be considered as the primary access site for all patients [11]. The incidence of technical complications associated with SCV insertion is high [2, 4–6]. The major complications of central venous catheterization may prove to be serious, particularly in critically ill patients. When the right IJV is not available for CVC, the second access site remains variable. Before utilization of the SCV, the EJV should be used [4, 7]. The benefits inherent in the use of the EJV include its large size and a greater ability to accommodate larger or multilumen catheters more easily than many peripheral insertion sites, the superficial location, the ability to visualize the EJV and the ease of access in reaching the SVC. The technique of central venous catheterization via the EJV was reported in 1974 [10]. The EJV approach has not been popular because of its low success rate [16], which is due to further anatomical considerations. The temporal and occipital veins drain into to EJV. The EJV flows in a curved and nonfixed course through the neck from the angle of the mandible obliquely to the base of the neck. At lower segments of the EJV, the AJV, TCV, and SSV drain to the EJV at the entrance to SCV, the EJV runs in a lateral direction, potentially leading to the arm rather than the thorax. In approximately 4% of the population, there is a plexus of veins under the clavicle [17]. Variations of these veins at the terminal point and angulation of the EJV to the SCV contribute to the insertion failure rate [10]. The EJV has two sets of valves, one at the entrance to the SCV and the other located 4 cm above the clavicle. These conditions cause difficulty in withdrawing catheters that have become kinked or

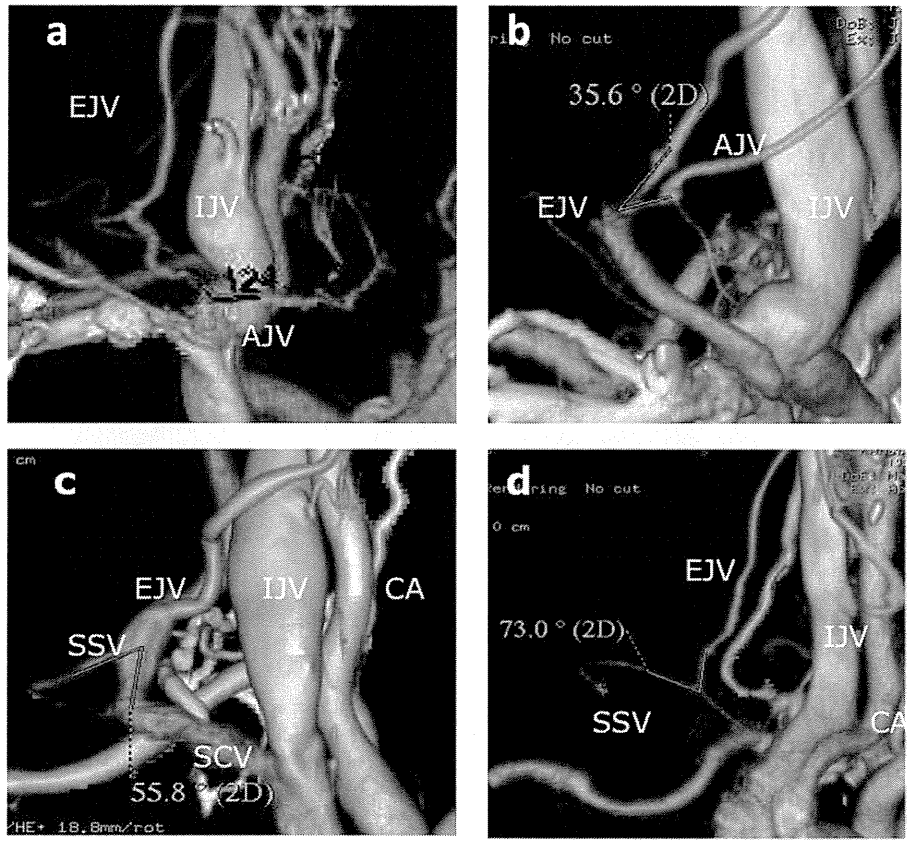

FIGURE 2 (a–d) MDCT venography: AP VR images. The CT-V showed the sharp angulation between the EJV and the AJV (a), and the EJV–AJV obtuse type (b). The sharp anglulation between the EJV and the SSV/TCV (c), and the EJV-TCV/SSC obtuse type (d).

knotted in the EJV [18]. Catheterization from the EJV requires a detailed anatomical orientation of these vessels including the central vascular system before the insertion procedure. Three-dimensional CT-V using MDCT clearly revealed individual vascular anomalies around the EJV and the SCV junction and could play an important role in safe cannulization. In our study, the angulation between the EJV and the TCV/SSV was most responsible for insertion success. Multiple access sites may be required to identify a suitable vein for central access. The CT-V can be an excellent tool for preprocedural mapping in more difficult venous access patients (4). MDCT venography has been shown to be as accurate as digital subtraction venography in central venous mapping [19, 20]. In some cases, the major problem encountered in threading an intravenous catheter through the EJV into the SCV without using a guide wire is the inability to pass the venous valve and the acute angles of tortuous veins. The J-wire easily transverses tortuous vessels, slides past valves, and navigates sharp angles [11]. When compared with the IJV or SCV sites, the EJV site offers a small risk of bleeding, puncture of the carotid artery, or pneumothorax in frail, elderly patients [10, 11, 21–24]. In this study, CT-V could not identify the left IJV, the EJV, or the right EJV in one case. The Doppler color ultrasound demonstrated significantly turbulent flow with decreased flow velocity of the left IJV. We could find this problem, which might cause complications with preoperative CT-V. Before utilization of the opposite side of IJV, the EJV should be used after the accurate estimation of condition of those vessels. Our results demonstrate percutaneous EJV cannulation to be safe for central venous access, with a high success rate compared with other sites [10, 11, 24]. However, it should be noted that the superficial location of the EJV and the small amount of subcutaneous tissue over the EJV may lead oozing of the blood. A short time simple manual compression can control subcutaneous oozing [11]. Superficial hematoma was the only problem found with the EJV route, and it was observed most often in the failed attempts. The site for percutaneously inserted catheters is determined by multiple factors, including the clinical status of patients, the purpose of central access, anticipated length of time it will be needed, and physician experience [25]. However, because of its high cost (CT-V cost: $238) and limited availability, the described procedure is not yet used for the routine diagnosis of venous

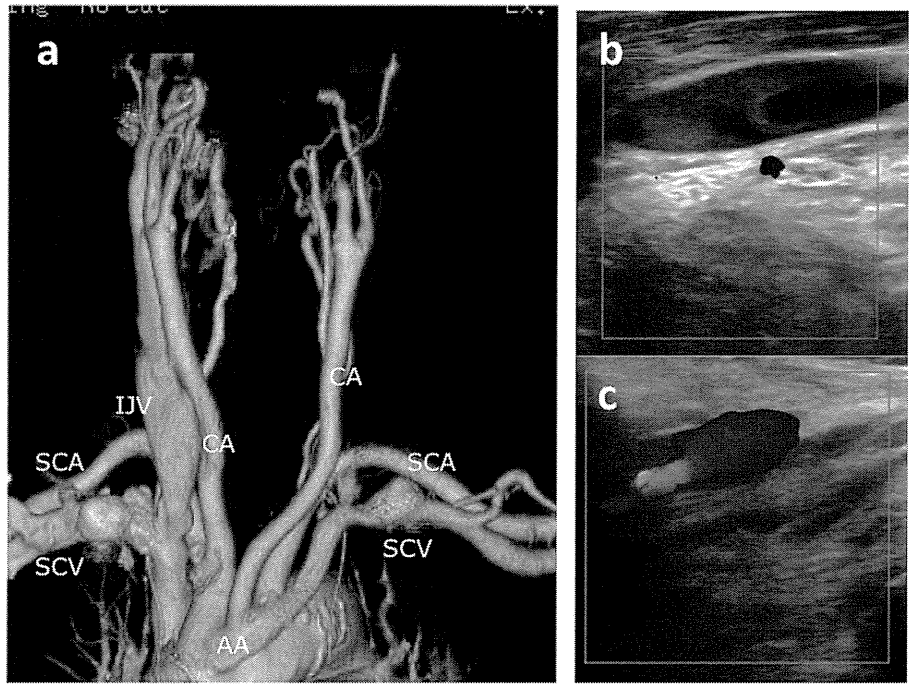

FIGURE 3 (a) MDCT venography and echo study: AP VR images. The CT-V could not identify the left IJV, the EJV, or the right EJV. The disappearance of the left IJV on CT-V image is characteristic. (b) Flow is demonstrated in the proximal section of the IJV and SCV by an ultrasound study. The Doppler color ultrasound demonstrates significantly turbulent flow with decreased flow velocity of the left IJV (c). No thrombosis was detected.

occlusion or estimation of the detailed anatomical orientation of the cervical venous plexus. The most important advantage is the absence of major complications. In regard to related patient safety, it is worth nothing that in the relatively recent past the use peripherally inserted central catheters has obviated some of the risks involved with more central access sites. Therefore, central venous access via the EJV seems to be an option to consider for vascular access in patients given our findings of a high success rate and a low complication rate [24]. The number of cases of reported is relatively small, which implies the need for a study involving a large patient population that would permit more precise assessment. Further studies are needed to determine how these advances in central access with compare to the safety profile of EJV technique.

CONCLUSIONS

Three-dimensional CT-V using MDCT clearly revealed individual vascular anatomies around EJV–SCV junction including the cervical venous plexus and could play an important role in safe cannulization. The EJV route is associated with comparable technical success and lower major procedural complication. The EJV approach with CT-V guidance is an option when central venous cannulation must be performed in patients under suboptimal conditions and patients in whom serious complications may prove to be fatal and with previous multiple central venous cannulations, especially those in hemodialysis or with long catheter indwelling periods, since because they are at higher risk of central venous occlusion.

Declaration of interest: The authors report no conflict of interest. The authors alone are responsible for the content and writing of the article.

No funds supported this study. Written informed consent was obtained from the patients for publication of this manuscript and any accompanying images. Copies of the written consent are available for review by the Editor-in-Chief of this journal.

REFERENCES

[1] Gorman RC, Buzby GP. Difficult access problems. *Surg Oncol Clin North Am.* 1995;4:453–472.
[2] Trerotola SO. You are asked to place a dialysis access catheter in a patient. What is your preferred access site, and why? *J Vasc Interv Radiol.* 1997;8:75–76.
[3] Susan NW. Unconventional venous access. *Tech Vas Interv Radiol.* 2001;5:114–120.
[4] Macdonald S, Watt AJB, McNally D, et al. Comparison of technical success and outcome of tunneled catheters inserted via the jugular and subclavian approach. *JVIR* 2000;11:225–231.

[5] Schillinger F, Schillinger D, Montagnac R, et al. Post catheterization vein stenosis in haemodialysis: comparative angiographic study of 50 subclavian and 50 internal jugular access. *Nephrol Dial Transplant.* 1991;6:722–7124.
[6] Moss AH, MacLaughlin MM, Lempert KD, et al. Use of a silicone catheter with a Dacron cuff for dialysis short-term vascular access. *Am J Kidney Dis.* 1988;12:492–489.
[7] Cimochowski GF, Worley E, Rutherford WE, et al. Superior of the internal jugular over the subclavian access for temporary dialysis. *Nephron.* 1990;54:154–161.
[8] Trerotola SO, Kuhn-johnson J, Johnson MS, et al. Tunneled infusion catheters: increased incidence of symptomatic venous thrombosis after subclavian versus internal jugular venous access. *Radiology* 2000;217:89–93.
[9] Forauer AR, Brenner B, Haddad LF, et al. Placement of hemodialysis catheters through dilated external jugular and collateral veins in patients with internal jugular vein occlusions. *AJR* 2000;174:361–362.
[10] Blitt CD, Wright WA, Petty WC, et al. Central venous catheterization via external jugular vein. *JAMA* 1974;229:817–818.
[11] Cho SK, Shin SW, Do YS, et al. Use of the right external jugular vein as the preferred access site when the right internal jugular vein is not usable. *J Vasc Interv Radiol.* 2006;17: 823–829.
[12] Finley GA. A complication of external jugular vein catheterization in children. *Can J Anaesth.* 1988;35:536–537.
[13] McCowan TC, Ferris EJ, Carver DK, et al. Use of external jugular vein as a route for percutaneous inferior vena cava filter placement. *Radiology* 1990;176;527–530.
[14] Byth PL. Evaluation of the technique of central venous catheterization via external jugular vein using J-wire. *Anaeth Intens Care* 1985;13:131–133.
[15] Shih YC, Chien HL, Hao MC, et al. A safe and effective method to implantable access port in patients with synchronous bilateral mastectomies: modified femoral vein approach. *J Surg Oncol.* 2008;98:197–199.
[16] Malatinsky J, Kadlic T, Majek M, et al. Misplacement and loop formation of central venous catheters. *Acta Anaesth Scand.* 1976;20:237–247.
[17] McKenzie BJ, Hatto IP. Difficult removal of external jugular vein catheters. *Anaesth Intens Care* 1981;9:158–160.
[18] Bita FF, Obeid M, Dabbous I, et al. Acute respiratory distress associated with external jugular vein catheterization in the newborn. *Pediar Pulmonol.* 2003;36:549–550.
[19] Heye S, Maleux G, Claes K, et al. Stenosis detection in native hemodialysis fistulas with MDCT angiography. *Am J Roentgenol.* 2009;192:1079–1084.
[20] Virmani V, Khandelwal N, Kang M, et al. MDCT venography in the evaluation of inferior vena cava in Budd-Chiari syndrome. *Indian J Gastroenterol.* 2009;28:17–23.
[21] Humphrey MJ, Bitt CD. Central venous access in children via external jugular vein. *Anesthesiology* 1982;57:50–51.
[22] Jobes DR, Schwartz AJ, Greenhow DE, et al. Safer jugular vein cannulation: recognition of arterial puncture and preferential use of the external jugular route. *Anesthesiology* 1983;59:353–355.
[23] Belani KG, Buckley JJ, Gordon JR, et al. Percutaneous cervical central venous line placement: a comparison of the internal and external vein routes. *Anetsh Analg.* 1980;59:40–44.
[24] Tecklenburg FW, Cochran JB, Webb SA, et al. Central venous access via external jugular vein in children. *Pediatr Emerg Care* 2010;26:554–557.
[25] de Jonge RC, Poldermann K, Gemke RJ. Central venous catheter use in the pediatric patient: mechanical and infectious complications. *Pediatr Crit Care Med.* 2005;6:329–333.

Hindawi Publishing Corporation
BioMed Research International
Volume 2013, Article ID 879491, 5 pages
http://dx.doi.org/10.1155/2013/879491

Clinical Study

Infliximab Extends the Duration until the First Surgery in Patients with Crohn's Disease

Aki Sakatani,[1] Mikihiro Fujiya,[1] Takahiro Ito,[1] Yuhei Inaba,[1] Nobuhiro Ueno,[1] Shin Kashima,[1] Motoya Tominaga,[1] Kentaro Moriichi,[1] Kotaro Okamoto,[1] Hiroki Tanabe,[1] Katsuya Ikuta,[1] Takaaki Ohtake,[1] Toru Kono,[2] Hiroyuki Furukawa,[2] Toshifumi Ashida,[3] and Yutaka Kohgo[1]

[1] *Division of Gastroenterology and Hematology/Oncology, Department of Medicine, Asahikawa Medical University, 2-1 Midorigaoka-higashi, Asahikawa, Hokkaido 078-8510, Japan*
[2] *Division of Gastroenterological and General Surgery, Department of Surgery, Asahikawa Medical University, 2-1 Midorigaoka-higashi, Asahikawa, Hokkaido 078-8510, Japan*
[3] *Department of Gastroenterology, Sapporo Higashi Tokushukai Hospital, 3-1 North 33-jou East 14-chome East Ward, Sapporo, Hokkaido 065-0033, Japan*

Correspondence should be addressed to Mikihiro Fujiya; fjym@asahikawa-med.ac.jp

Received 16 July 2013; Revised 19 October 2013; Accepted 20 October 2013

Academic Editor: Hidekazu Kuramochi

Background/Aims. While biological drugs are useful for relieving the disease activity and preventing abdominal surgery in patients with Crohn's disease (CD), it is unclear whether the use of biological drugs in CD patients with no history of abdominal surgery is appropriate. We evaluated the effects of infliximab and other factors on extending the duration until the first surgery in CD patients on a long-term basis. *Methods.* The clinical records of 104 CD patients were retrospectively investigated. The cumulative nonoperation rate until the first surgery was examined with regard to demographic factors and treatments. *Results.* The 50% nonoperative interval in the 104 CD patients was 107 months. The results of a univariate analysis revealed that a female gender, the colitis type of CD, and the administration of corticosteroids, immunomodulators, or infliximab were factors estimated to improve the cumulative nonoperative rate. A multivariate analysis showed that the colitis type and administration of infliximab were independent factors associated with a prolonged interval until the first surgery in the CD patients with no history of abdominal surgery. *Conclusions.* This study suggests that infliximab treatment extends the duration until the first surgery in CD patients with no history of abdominal surgery. The early use of infliximab before a patient undergoes abdominal surgery is therefore appropriate.

1. Introduction

Crohn's disease (CD) is a chronic inflammatory bowel disease whose etiology remains unclear. Deep and refractory ulcers frequently develop in the small intestine in CD patients, often causing severe complications, including abdominal abscesses and ileus. Open surgery is sometimes required to relieve the patient's conditions, including ileus due to severe stricture, refractory abscesses, and fistulas, which lead to a deterioration of the general condition and quality of life in the patients, as well as severe intestinal bleeding [1]. Recent advances in therapeutic strategies have led to the development of biological agents, such as infliximab and adalimumab, that have improved the success rate of inducing remission and are useful as maintenance therapy in patients with refractory CD [2–6]. The administration of biological agents also reduces the rate of complications and extends the duration from the first to the second surgery [7–10]. Because the traditional therapeutic approach for treating CD is based on a step-up strategy [11], the administration of treatment with biological drugs is recommended in patients who fail to respond to conventional therapy, but not patients who exhibited mild to moderate disease activity without a history of abdominal surgery. Recently, D'Haens et al. reported in a 2-year randomized trial that the percentage of newly diagnosed patients without a need for corticosteroid

treatment or surgery at six and 12 months was significantly higher in the group administered infliximab [12]. This short-term observation suggests that the use of infliximab in CD patients, who were diagnosed within the past four months, can increase the duration of remission and extend the duration until the first surgery. Conversely, Jones and Finlayson evaluated the Nationwide Inpatient Sample in the US and concluded that, during the period of adoption of infliximab as a novel CD treatment, the overall rate of bowel resection either remained relatively stable or moderately decreased [13]. Domènech et al. retrospectively reviewed the clinical outcomes of newly diagnosed Crohn's disease patients before and after infliximab availability and concluded that infliximab availability did not reduce the need for surgery or the development of disease-related complications [14]. It remains unclear whether the early use of biological drugs decreases the risk of the first surgery in CD patients.

The present retrospective study investigated factors affecting the interval from the time of diagnosis to the first surgery, including patient demographics, type of disease, and treatment procedures, in CD patients with no history of abdominal surgery.

2. Methods

2.1. Patients. Written informed consent was obtained from all identified patients, and the study was approved by the institutional review board of Asahikawa Medical University. The clinical records of 104 patients who were diagnosed as having CD at Asahikawa Medical University between February 1982 and October 2011 were retrospectively investigated. The diagnosis of CD was made based on the combination of the clinical course and the colonoscopy, double balloon endoscopy, small bowel enterolysis, and histological findings. Typical lesions of CD, including longitudinal ulcers and a cobblestone appearance in the small and/or large intestine, were observed on endoscopy in all patients. Intestinal strictures, fistula formation, and abdominal abscesses were also observed in the patients. These findings were also referenced for the diagnosis of CD. Data regarding patient demographics, treatments, and operative findings were collected by A.S., who did not participate in the diagnosis, medical examination, or treatment of the patients. The onset of the disease was defined as the time of appearance of symptoms caused by CD. The date of disease onset was used to divide the patients into two groups, those treated before 2001 and those treated after 2002, because infliximab became clinically available in Japan in 2002. Patients who received infliximab four or more times, corticosteroids as remission induction therapy, or immunomodulators for one or more months were classified as belonging to the infliximab-positive, corticosteroid-positive, or immunomodulator-positive groups, respectively. These agents were administered in patients resistant to 5-aminosalicylate treatment and/or those who requested these drugs.

2.2. Cumulative Nonoperative Rate until the First Surgery. The abdominal surgeries performed in this study included intestinal resection, strictureplasty, colostomy, and ileostomy. The demographic and treatment-related factors were retrospectively compared with the cumulative nonoperative rate until the first surgery. In the patients who did not undergo surgery, the interval from diagnosis to the end of the study was defined as the nonoperative time (March 2012). In the patients who underwent either single or multiple surgeries, the interval from diagnosis to the first surgery was defined as the nonoperative time.

2.3. Statistical Analyses. The Kaplan-Meier method was used to test the cumulative nonoperative rates and the data related to each factor were statistically analyzed using the log-rank test. A Cox proportional hazards model was used to calculate the hazard ratios of the factors identified to estimate the frequency of surgery. A P value of <0.05 was considered to be statistically significant (two-sided test).

3. Results

3.1. Patient Demographics and Treatments. Seventy-one male and 33 female patients were included in this study. Sixty-seven (64%) patients exhibited lesions in both the small and large intestines (ileocolitis type), 28 (27%) patients had lesions in the small intestine only (ileitis type), and nine (9%) patients had lesions in the large intestine only (colitis type). The age at disease onset ranged from 10 to 66 years, with a median of 22 years. The date of disease onset was before 2001 in 74 patients and after 2002 in 30 patients. Corticosteroids, immunomodulators, and infliximab were administered in 33 (32%), 37 (36%), and 39 (38%) of the patients before the first surgery, respectively. A total of 16 of the 74 patients who had disease onset before 2001 and 23 of the 30 patients who had disease onset after 2002 took infliximab. Sixty-nine patients (66%) underwent one or more surgeries (Table 1). A total of 134 surgeries were performed. Ileal or jejunal resection was performed in 76 patients, strictureplasty was performed in 10 patients, and colostomy or ileostomy was performed in six patients. Combination surgeries were performed in 42 patients (Table 2).

3.2. Clinical Factors Associated with the Cumulative Nonoperative Rate. The cumulative nonoperative rate among all 104 patients is shown in Figure 1. The 50% nonoperative interval was 107 months. The relationships between the clinical factors, such as gender, the location of the lesions, the age at disease onset and treatments, and the cumulative nonoperative rate, were analyzed. The results of a univariate analysis of the cumulative nonoperative rate based on the presence or absence of each clinical factor are shown in Table 3. The analysis revealed that a female gender, the colitis type of CD, and the administration of corticosteroids, immunomodulators, or infliximab were factors estimated to improve the cumulative nonoperative rate (Figure 2). A multivariate analysis showed the colitis type of CD and the administration of infliximab to be independent factors associated with a prolonged interval until the first surgery. The hazard ratios of the colitis type of CD and the administration

Table 1: Patient demographics and treatments (104 cases).

	Number of patients (n = 104)
Sex	
Male	71 (68%)
Female	33 (32%)
Type of disease	
Ileitis	28 (27%)
Ileocolitis	67 (64%)
Colitis	9 (9%)
The age of onset	
Median	22
Range	10–66
The history of corticosteroid use until the first operation	
(+)	33 (32%)
(−)	71 (68%)
The history of immunomodulator use until the first operation	
(+)	37 (36%)
(−)	67 (64%)
The history of infliximab use until the first operation	
(+)	39 (38%)
(−)	65 (62%)
The history of enteral nutrition	
(+)	96 (92%)
(−)	8 (8%)
Bowel surgery	
(+)	69 (66%)
(−)	35 (34%)

of infliximab were 0.086 (0.011–0.657) and 0.256 (0.122–0.540), respectively (Table 4).

4. Discussion

The present study showed that the administration of infliximab extends the duration until the first surgery in CD patients who have not previously undergone abdominal surgery. This suggests that the administration of infliximab is useful in CD patients with no experience with abdominal surgery. While the usefulness of biological drugs for inducing and maintaining remission of CD and extending the duration from the first to the second surgery has been established [2, 3, 10], it remains unclear whether these biological drugs should be administered in CD patients with no history of abdominal surgery. Recently, D'Haens et al. reported in a 2-year open-label-randomized trial that the percentage of CD patients who were diagnosed within four months in clinical remission and were neither receiving corticosteroids nor requiring surgery at six and 12 months was significantly higher in the group treated with infliximab [12], thus suggesting that the early use of infliximab can improve the short-term outcomes of CD. The present study supports the notion that infliximab treatment can improve both the long-term and short-term outcomes in CD patients, even when the patient has no history of abdominal surgery.

Table 2: Surgical procedures performed in 69 patients with Crohn's disease (total: 134 operations).

	Total of 134 operations
Bowel resection	76
Strictureplasty	10
Colostomy or ileostomy	6
Bowel resection and strictureplasty	27
Bowel resection and colostomy (or ileostomy)	13
Strictureplasty and colostomy (or ileostomy)	1
Bowel resection and strictureplasty and colostomy (or ileostomy)	1

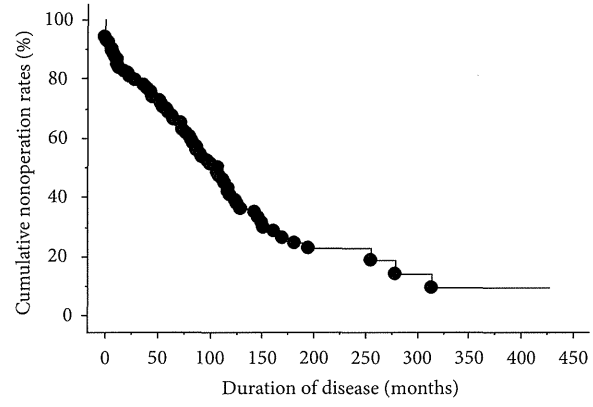

Figure 1: The cumulative nonoperative rate among all 104 patients. The nonoperative rate was inversely proportional to the duration of the disease.

Although the present study demonstrated the efficacy of infliximab treatment, the period of disease onset may have influenced the duration from disease onset to the first surgery. After 2002, the availability of infliximab treatment is not the only factor that changed from the previous era. The types and characteristics of microorganisms causing infectious colitis and the eating habits and lifestyle factors affecting the pathology of inflammatory diseases have been changed over the past two decades in Japan. Therefore, the present study investigated the influence of the date of disease onset on the duration until the first surgery, the results of which showed that the date of disease onset is not a significant factor affecting the duration until the first surgery in CD patients. An evaluation of the Nationwide Inpatient Sample conducted in the US concluded that, during the period of adoption of infliximab as a novel CD treatment, the overall rate of bowel resection either remained relatively stable or moderately decreased [13]. Domènech et al. also reviewed the clinical

Table 3: Factors associated with the nonoperative rate until the first surgery (univariate analysis).

	Number of patients (n = 104)	50% nonoperation time (months)	P value
Sex			
Male	71	84	<0.05
Female	33	142	
Type of disease			
Ileitis/ileocolitis	95	98	<0.05
Colitis	9	Undefined	
The age of onset			
Less than 20	39	117	N.S.
20 or more	65	98	
The date of onset			
Before 2001	74	107	N.S
After 2002	30	Undefined	
Corticosteroid			
(+)	33	126	<0.05
(−)	71	91	
Immunomodulator			
(+)	37	169	<0.05
(−)	67	84	
Infliximab			
(+)	39	256	<0.05
(−)	65	78	

Undefined: nonoperation time is greater than 50% at the last time point. N.S.: not significant.

Table 4: Factors associated with the nonoperative rate until the first surgery (multivariate analysis).

		Hazard ratio	95% CI
Sex	Female	0.605	0.339–1.081
Type of disease	Colitis	0.086	0.011–0.657
Corticosteroid	(+)	0.912	0.519–1.604
Immunomodulator	(+)	1.057	0.569–1.966
Infliximab	(+)	0.256	0.122–0.540

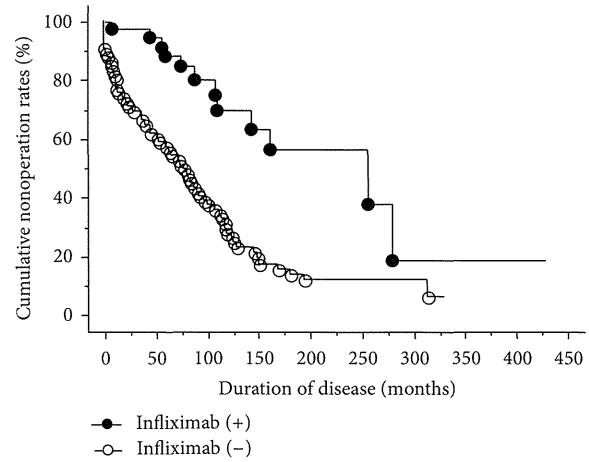

Figure 2: The results of a univariate analysis of the cumulative nonoperative rate based on the presence or absence of infliximab treatment. The univariate analysis revealed that the administration of infliximab is a factor estimated to improve the cumulative nonoperative rate.

outcomes of newly diagnosed Crohn's disease patients before and after infliximab availability in a retrospective study and concluded that infliximab availability did not reduce the need for surgery [14]. These investigations and the present study therefore indicate that the date of disease onset is not a strong factor affecting the duration until the first surgery in CD patients. Further long-term prospective studies of large numbers of CD patients with no history of abdominal surgery are needed to confirm the significance of biological agents in improving the cumulative nonoperative rate in CD patients.

In this study, while the univariate analysis revealed that the administration of corticosteroids and immunomodulators affected the duration until the first surgery, the multivariate analysis did not identify these treatments to be independent factors. Therefore, these therapies are not very useful for treating CD patients with no history of abdominal surgery in comparison to the administration of infliximab. The administration of corticosteroids has been shown to be effective for inducing remission in patients with CD [15–20]. However, it is well known that the administration of corticosteroids is associated with various side effects. Corticosteroids should be used as short-term therapy only when other treatments are ineffective. Although the administration of immunomodulators alone is useful for maintaining CD [21, 22], combination therapy with immunomodulators and infliximab has been shown to be more effective for this purpose [23]. Because immunomodulators were used in combination with infliximab in most cases in the present study,

the multivariate analysis did not identify immunomodulators to be an independent factor.

In summary, the results of the present study suggest that infliximab treatment has the potential to extend the duration until the first surgery. This implies that the administration of infliximab in CD patients with no history of abdominal surgery, even in CD patients with no experience with abdominal surgery, can improve the outcomes, including the cumulative nonoperative rate. Further randomized, controlled trials are needed to establish the appropriate timing of the initiation of infliximab treatment and determine the optimal dose, schedule, and duration of the administration of these biological drugs.

Conflict of Interests

The authors declare that they have no conflict of interests.

Authors' Contribution

Aki Sakatani and Mikihiro Fujiya contributed equally to this study.

References

[1] O. Bernell, A. Lapidus, and G. Hellers, "Risk factors for surgery and postoperative recurrence in Crohn's disease," *Annals of Surgery*, vol. 231, no. 1, pp. 38–45, 2000.

[2] S. B. Hanauer, B. G. Feagan, G. R. Lichtenstein et al., "Maintenance infliximab for Crohn's disease: the ACCENT I randomised trial," *The Lancet*, vol. 359, no. 9317, pp. 1541–1549, 2002.

[3] P. Rutgeerts, B. G. Feagan, G. R. Lichtenstein et al., "Comparison of scheduled and episodic treatment strategies of infliximab in Crohn's disease," *Gastroenterology*, vol. 126, no. 2, pp. 402–413, 2004.

[4] B. G. Feagan, R. Panaccione, W. J. Sandborn et al., "Effects ofadalimumab therapy on incidence of hospitalization and surgery in Crohn's disease: results from the CHARM Study," *Gastroenterology*, vol. 135, no. 5, pp. 1493–1499, 2008.

[5] J.-F. Colombel, W. J. Sandborn, P. Rutgeerts et al., "Adalimumab for maintenance of clinical response and remission in patients with Crohn's disease: the CHARM trial," *Gastroenterology*, vol. 132, no. 1, pp. 52–65, 2007.

[6] S. B. Hanauer, W. J. Sandborn, P. Rutgeerts et al., "Human anti-tumor necrosis factor monoclonal antibody (adalimumab) in Crohn's disease: the CLASSIC-I trial," *Gastroenterology*, vol. 130, no. 2, pp. 323–332, 2006.

[7] G. R. Lichtenstein, S. Yan, M. Bala, M. Blank, and B. E. Sands, "Infliximab maintenance treatment reduces hospitalizations, surgeries, and procedures in fistulizing Crohn's disease," *Gastroenterology*, vol. 128, no. 4, pp. 862–869, 2005.

[8] F. Schnitzler, H. Fidder, M. Ferrante et al., "Long-term outcome of treatment with infliximab in 614 patients with Crohn's disease: results from a single-centre cohort," *Gut*, vol. 58, no. 4, pp. 492–500, 2009.

[9] J. K. Bhatia, B. I. Korelitz, G. Panagopoulos et al., "A prospective open-label trial of Remicade in patients with severe exacerbation of Crohn's disease requiring hospitalization: a comparison with outcomes previously observed in patients receiving intravenous hydrocortisone," *Journal of Clinical Gastroenterology*, vol. 41, no. 7, pp. 677–681, 2007.

[10] M. Regueiro, W. Schraut, L. Baidoo et al., "Infliximab prevents Crohn's disease recurrence after ileal resection," *Gastroenterology*, vol. 136, no. 2, pp. 441.e1–450.e1, 2009.

[11] A. Dignass, G. Van Assche, J. O. Lindsay et al., "The second European evidence-based consensus on the diagnosis and management of Crohn's disease: current management," *Journal of Crohn's and Colitis*, vol. 4, no. 1, pp. 28–62, 2010.

[12] G. D'Haens, F. Baert, G. van Assche et al., "Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn's disease: an open randomised trial," *The Lancet*, vol. 371, no. 9613, pp. 660–667, 2008.

[13] D. W. Jones and S. R. G. Finlayson, "Trends in surgery for crohn's disease in the era of infliximab," *Annals of Surgery*, vol. 252, no. 2, pp. 307–312, 2010.

[14] E. Domènech, Y. Zabana, E. Garcia-Planella et al., "Clinical outcome of newly diagnosed Crohn's disease: a comparative, retrospective study before and after infliximab availability," *Alimentary Pharmacology and Therapeutics*, vol. 31, no. 2, pp. 233–239, 2010.

[15] S. C. Truelove and L. J. Witts, "Cortisone in ulcerative colitis; preliminary report on a therapeutic trial," *British Medical Journal*, vol. 2, no. 4884, pp. 375–378, 1954.

[16] R. W. Summers, D. M. Switz, and J. T. Sessions Jr., "National cooperative Crohn's disease study: results of drug treatment," *Gastroenterology*, vol. 77, no. 4, pp. 847–869, 1979.

[17] H. Malchow, K. Ewe, and J. W. Brandes, "European cooperative Crohn's disease study (ECCDS): results of drug treatment," *Gastroenterology*, vol. 86, no. 2, pp. 249–266, 1984.

[18] G. R. Greenberg, B. G. Feagan, F. Martin et al., "Oral budesonide for active Crohn's disease," *The New England Journal of Medicine*, vol. 331, no. 13, pp. 836–841, 1994.

[19] M. Campieri, A. Ferguson, W. Doe, T. Persson, and L.-G. Nilsson, "Oral budesonide is as effective as oral prednisolone in active Crohn's disease," *Gut*, vol. 41, no. 2, pp. 209–214, 1997.

[20] O. Ø. Thomsen, A. Cortot, D. Jewell et al., "A comparison of budesonide and mesalamine for active Crohn's disease," *The New England Journal of Medicine*, vol. 339, no. 6, pp. 370–374, 1998.

[21] D. H. Present, B. I. Korelitz, and N. Wisch, "Treatment of Crohn's disease with 6-mercaptopurine. A long-term, randomized, double-blind study," *The New England Journal of Medicine*, vol. 302, no. 18, pp. 981–987, 1980.

[22] S. Candy, J. Wright, M. Gerber, G. Adams, M. Gerig, and R. Goodman, "A controlled double blind study of azathioprine in the management of Crohn's disease," *Gut*, vol. 37, no. 5, pp. 674–678, 1995.

[23] J. F. Colombel, W. J. Sandborn, W. Reinisch et al., "Infliximab, azathioprine, or combination therapy for Crohn's disease," *The New England Journal of Medicine*, vol. 362, no. 15, pp. 1383–1395, 2010.