Novel Balloon Pulmonary Angioplasty Technique for Chronic Thromboembolic Pulmonary Hypertension

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Summary

This study aimed to clarify the usefulness of the Ikari-curve left (IL) guiding catheter for balloon pulmonary angioplasty (BPA).

The current BPA strategy for chronic thromboembolic pulmonary hypertension is dilation of as many branches as possible to normalize hemodynamics and oxygenation. The shape of the guiding catheter is a major factor in achieving this. However, conventional guiding catheters are difficult to introduce into particular branches. The IL guiding catheter may be suitable; however, its utility remains unclear.

We retrospectively analyzed 202 consecutive BPA sessions of 40 patients from November 2016 to October 2019 and divided these sessions into two groups: the IL group where the IL guiding catheter was used and the non-IL group where other catheters were utilized. The occurrence of lung injury was determined by the presence of bloody sputum. We compared the rates of successful introduction into target vessels and assessed for the occurrence of lung injury.

The average age of enrolled patients was 60.3 ± 14.4 years, with females comprising 65%. There were 99 sessions in the IL group. The median treated branches per session differed between the 2 groups (IL group: 15 versus non-IL group: 10, \( P < 0.05 \)). The occurrence of lung injury was lower in the IL group (4.0% versus 11.7%, \( P = 0.07 \)). The IL group had more successful vessel insertions than the non-IL group (78.8% versus 42.7%, \( P < 0.01 \)).

The IL guiding catheter may be introduced into branches that cannot be accessed by conventional guiding catheters.

Key words: Pulmonary embolism, Interventional devices/innovation, Ikari-curve left (IL) guiding catheter

C hronic thromboembolic pulmonary hypertension (CTEPH) occurs when organized thrombi restrict pulmonary arterial blood flow. Even though this disease is rare, its accurate diagnosis is necessary because it is treatable. The prognosis of CTEPH is markedly worse for patients with a mean pulmonary artery pressure (mPAP) more than 30 mmHg. Therefore, the conventional goal of treatment is improvement of the mPAP to a value less than 30 mmHg. Balloon pulmonary angioplasty (BPA) has been a popular therapeutic option for inoperable CTEPH management. It underwent technical refinement in 2012 and achieved treatment goals in inoperable Japanese CTEPH patients. Nevertheless, some patients have limitations in their activities due to residual exertional hypoxia despite having an mPAP less than 25 mmHg. This suggests that hypoxia due to residual ventilation-perfusion mismatch may contribute to the symptoms and the quality of life. The current goal of treatment is to improve not only the hemodynamic status, but also the oxygenation by eliminating ventilation-perfusion mismatch. In light of this goal, the BPA technical method was further refined. Treating as many branches as possible became a priority in each session. In BPA, an 8-Fr sheath is placed into the femoral or internal jugular vein. A 6-Fr sheath is then introduced into the pulmonary artery trunk via the 8-Fr sheath using a 0.035-inch wire. Next, the vessel is selected by inserting a 6-Fr guiding catheter through the 6-Fr sheath.

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in a previous report.\textsuperscript{13} The difficulty of successfully inserting into these vessels made a difference in terms of the degree of dilation between branches. Existence of residual lesions resulted in a ventilation-perfusion mismatch deterioration despite the improved hemodynamics.\textsuperscript{9} The shape of the guiding catheter suitable for introduction into these branches has remained unknown. The Ikari-curve (IL) catheter (Terumo\textsuperscript{TM}, Tokyo) is a modification of the Judkins L catheter. It has 4 curves originally designed for percutaneous coronary intervention via the radial access.\textsuperscript{14} The universal IL guiding catheter has been successfully used for both the right and left coronary arteries.\textsuperscript{15} We hypothesized that the IL guiding catheter could be introduced into such branches by adjusting its curves through the use of a long-sheath catheter. The aim of this study was to determine the ability of the IL guiding catheter in accessing these vessels.

Methods

Study design: We conducted a retrospective, observational study to evaluate the usefulness of IL guiding catheter in performing BPA at the University of Tokyo Hospital. This study was approved by the University of Tokyo Hospital Review Board for clinical research (No. 2650).

Patients: This study was conducted from November 2016 to October 2019. Within this period, a total of 202 BPA sessions were performed in 40 patients. We divided the BPA sessions into two groups: the IL group which used the IL guiding catheter in its sessions; and, the non-IL group which did not utilize the IL guiding catheter. Starting in November 2016, we used IL guiding catheters in patients who underwent an initial BPA for the left lung. Similarly, IL guiding catheters for BPA sessions done on the right pulmonary artery were used starting in December 2018. Whenever it was impossible to penetrate the above-mentioned vessels using conventional guiding catheters, we opted to use IL guiding catheters in the subsequent sessions.

Balloon pulmonary angioplasty: The precise method of BPA was described in our previous report.\textsuperscript{12} In each BPA session, all areas of the lung on the side which treatment was planned were targeted. We introduced the IL guiding catheter into branches of the pulmonary artery (rt.A4+5, rt.A7, lt.A3, lt.A4+5, and lt.A8, number of treated vessels per session, fluoroscopic time, and amount of contrast medium) as well as the procedural safety (occurrence of lung injury) of each BPA session. Successful introduction into the target vessel was achieved when the guiding catheter was fully inserted into the vessel and balloon dilation was achieved.

Figure 1. Typical adjustments of the IL guiding catheter, long sheath (A-D), and angiograms (E-H). Adaptation shifts from the dorsal to the ventral branches are shown in A-D. The location of the pulmonary angiogram is seen in the posterior basal branch of the left pulmonary artery, lt. A10 (E); the lateral basal branch of the right pulmonary artery, rt. A9 (F); the lingular branches, lt. A4 + 5 (G); and, the medial basal branch of the right pulmonary artery, rt. A7 (H).
branches through the Judkins R catheter. Finally, an MP guiding catheter was introduced into the target branch through the Judkins R catheter. The technique was complicated and required many attempts. We calculated the average fluoroscopic time per treated branch by dividing the fluoroscopic time and the number of treated branches in each session. The occurrence of lung injury was determined by the presence of bloody sputum during the perioperative period. Bleeding from the pulmonary artery other than the rt.A4+5, rt.A7, lt.A3, lt.A4+5, and lt.A8 branches was also considered “lung injury”.

Statistical analysis: The results are expressed as the mean ± standard deviation (SD). Comparisons between the two groups were performed using the paired two-tailed t-test. The Wilcoxon signed rank test was used for ratio scales, while the chi-square and Fisher’s exact tests were used for nominal scales. A P value less than 0.05 was considered statistically significant. All statistical analyses were performed using Prism 7 for Windows (version 7.03; GraphPad, San Diego, CA, USA).

Results
Baseline characteristics: The baseline characteristics of the study patients and study design are shown in Table I and Figure 2, respectively. There were no significant differences among the characteristics. A total of 40 patients underwent BPA. Among the 202 BPA sessions, 99 involved the IL guiding catheter. There were 4 sessions in which we treated the pulmonary arteries of both lungs because the patients’ condition and hemodynamic status were stable. In these sessions, after finishing one lung, the amount of contrast medium and fluoroscopic time were minimal. The frequency of using the IL guiding catheter sequentially increased from only one session in 2016 to 10 sessions in 2017, 37 sessions by 2018, and eventually 51 sessions as of 2019.

Procedural results: The median number of treated branches per session was significantly larger in the IL group compared to the non-IL group (15 versus 10). The average fluoroscopic time and contrast medium amount did not significantly differ between the groups. However, in the IL group the average required fluoroscopic time per number of treated branches was significantly shorter than the non-IL group (4.4 ± 2.7 minutes versus 7.4 ± 8.0 minutes). Lung injury occurred more in the non-IL group; however, the difference was not significant. All cases of lung injuries occurred during the BPA procedure, and were treated by increasing the amount of oxygen inhalation (IL group: 1; non-IL group: 2), adding a wedge guiding catheter or balloon (IL group: 2; non-IL group: 8), and infiltrating a gelatin sponge (IL group: 1; non-IL group: 2). All patients achieved hemostasis and did not require mechanical ventilation with intratracheal intubation. The procedural results are shown in Table II.

Success rates of introduction into branches: Typical angiograms of IL guiding catheter insertion into rt. A4+5, rt. A7, lt. A3, lt. A4+5, and lt. A8 are shown in Figure 3. The conventional catheter had difficulty in successfully approaching these branches, as shown in Table III. The success rates of rt. A4+5, rt. A7, and lt. A4+5 in the IL group were significantly higher than the non-IL group (rt. A4+5: 84.4% versus 57.5 %; rt. A7: 46.9% versus 7.5%; and, lt. A4+5: 90.0% versus 62.5%). The success rates of lt. A3 and lt. A8 in the IL group were also higher; however, these differences were not significant (lt. A3: 82.9%...
The IL guiding catheter has the potential to be introduced into branches in which conventional guiding catheter access is difficult. Multiple branches may be treated in each session by the IL guiding catheter, thereby reducing the occurrence of lung injury. To the best of our knowledge, this is the first report on the effectiveness of the IL guiding catheter on BPA.

These results are thought to be compatible with the current BPA method of dilating as many branches as possible in each session. Selection of a guiding catheter can play an important role in achieving this objective. In fact, the median number of treated branches in one session was greater in the IL group than the non-IL group. It is possible that the time for introduction into each branch was shorter in the IL group due to the result of the average required fluoroscopic time per treated branch. This fact is important for safety concerns in BPA. When lung injury occurs, rapid hemostasis is most important. A rapid approach using the IL guiding catheter for targeting vessels has the potential to shorten the time needed to achieve hemostasis.

Table II. Procedural Results of BPA

| Side | IL group (n = 99) | Non-IL group (n = 103) | P value |
|------|------------------|------------------------|---------|
| Side | Rt. (29); Lt. (67); both (3) | Rt. (79); Lt. (23); both (1) |         |
| Type of guiding catheter | IL 3.0 (62); IL 3.5 (37) | MP (72); AL-1 (23); AL-2 (3); EBU3.0 (4); IMA (1) |         |
| Median number of treated branches | 15 | 10 | <0.0001 |
| Average amount of contrast medium (mL) | 124.3 ± 34.8 | 125.4 ± 44.4 | 0.85 |
| Average of fluoroscopy time (minutes) | 59.6 ± 15.8 | 59.9 ± 15.8 | 0.90 |
| Average of fluoroscopic time per treated branches (minutes) | 4.4 ± 2.7 | 7.4 ± 8.0 | 0.0005 |
| Lung injury (%) | 4 (4.0) | 12 (11.7) | 0.07 |

AL-1 indicates Amplatz left 1.0; AL-2, Amplatz left 2.0; BPA, balloon pulmonary angioplasty; EBU, extra-back-up; IL, Ikari left; It: left; IMA, Internal mammary artery; MP, multipurpose; and Rt, right.

Figure 3. Angiograms showing the introduction of the IL guiding catheter into rt. A4 + 5 (A and F), rt. A7 (B and G), lt. A3 (C and H), lt. A4 + 5 (D and I), and lt. A8 (E and J). The angiograms are taken from the anterior-posterior view (A-E) and left anterior oblique 60° view (F-J). IL indicates Ikari left; lt. A3, anterior ascending and descending branches of the left pulmonary artery; lt. A4 + 5, lingular branches; lt. A8, anterior basal branch of the left pulmonary artery; rt. A4 + 5, main branches of the middle lobe of the right pulmonary artery; and rt. A7, medial basal branch of the right pulmonary artery.

Table III. Success Rate of Introduction into Branches

|                   | Total | Rt. A4 + 5 | Rt. A7 | Lt. A3 | Lt. A4 + 5 | Lt. A8 |
|-------------------|-------|------------|--------|--------|------------|--------|
| IL guiding catheter (%) | 78.8* | 84.4* | 46.9* | 82.9 | 90.0* | 75.7 |
| Other guiding catheters (%) | 42.7 | 57.5 | 7.5 | 70.8 | 62.5 | 62.5 |

BPA indicates balloon pulmonary angioplasty; IL, Ikari left; lt. A3, anterior ascending and descending branches of left pulmonary artery; lt. A4 + 5, lingular branches; lt. A8, anterior basal branch of left pulmonary artery; rt. A4 + 5, main branches for middle lobe of right pulmonary artery; and rt. A7, medial basal branch of right pulmonary artery. *P < 0.05.

versus 70.8% in the non-IL group; and lt. A8: 75.7% versus 62.5%).

Discussion

The IL guiding catheter has the potential to be introduced into branches in which conventional guiding catheter access is difficult. Multiple branches may be treated in each session by the IL guiding catheter, thereby reducing the occurrence of lung injury. To the best of our knowledge, this is the first report on the effectiveness of the IL guiding catheter on BPA.
USEFULNESS OF THE IL-GUIDING CATHETER IN BPA

There are two points of discussion regarding the successful introduction into branches. First, the success rate of introduction into rt. A7 was the lowest among all other branches. This is because of the difficulty in distinguishing rt. A7 anatomically. It has been reported that 5.7%-6% of patients do not have an rt. A7, and 53.1% to 60% of patients have vessels branching from the common trunk to the anterior basal branch of the right pulmonary artery (rt. A8). The percentage of an independently branching rt. A7 is 34%-40.1%. Therefore, the rt. A7 may occasionally be counted as an rt. A8 because their distinction is made only by using pulmonary angiograms. Second, there were no significant differences among the success rates of lt. A3 and lt. A8. Even for lt. A4+5, the success rate of the non-IL group was higher than that of the right pulmonary arteries. This is because we routinely used an Amplatzer left 1.0 guiding catheter for introduction into these branches of the left pulmonary artery. We previously used the MP guiding catheter; however, it was quite difficult to introduce into rt. A4+5, rt. A7, lt. A3, lt. A4+5, and lt. A8. The technique has been elaborated in the Methods section. It was complicated and required many attempts. Furthermore, the MP guiding catheter often dislodged due to poor backup force. If a lung injury occurs in this situation, many attempts would be required to achieve hemostasis. This suggests that the conventional methods using the MP guiding catheter and the Judkins R catheter are not compatible with the current strategy of BPA in terms of safety and efficacy.

The occurrence of lung injury tended to be lower in the IL group because this catheter provides good stability and back up force after being introduced into the target branches.17,19 Almost all of the lung injuries occurred due to perforation of the guide wire distal to the small vessel. This was induced by the migration of the guide wire from a main branch to a smaller lateral branch.16,20 There are two reasons for this phenomenon: respiratory fluctuation of the guide wire and instability of the guiding catheter. We usually ask patients to maintain an inspiratory position when inserting the guide wire into a suitable position. However, after expiration, respiratory fluctuation sometimes induces shifting of the guide wire to other vessels. If the guide wire shifts to small vessels, this may cause lung injury. For this reason, we usually avoid inserting the guide wire into very distal positions. The result of this intervention is a weakened backup force. Sometimes, the balloon cannot pass through the lesion. The backup force can be enforced by using the IL guiding catheter because the catheter tip firmly fits into the ostium of branches. The curve of the IL guiding catheter also fits into the vessel wall on the opposite side of the branch in a linear fashion. Furthermore, once the guiding catheter has been stabilized, the guide wire also becomes firmly held in place. This further reduces the possibility of lung injury.

Our study has 5 limitations. First, it had a single-center, retrospective design and a small number of patients. Therefore, it may be subject to selection bias. Multi-center studies are needed to validate our findings. Second, almost of all the BPA sessions were performed by only one person (190 in 202 sessions). Third, the hemodynamics could not be compared between the groups because there were sessions which used both an IL guiding catheter and other guiding catheter types in the same patient. Nevertheless, the median number of BPA sessions was equal in both groups (4 in each group). Thus, the baseline hemodynamics might not have differed significantly. Fourth, our technical progress in BPA might have favored the IL group. The number of sessions in which the IL guiding catheter was used increased over time, while sessions using other kinds of catheters decreased. Fifth, the usefulness of other types of guiding catheters which had a similar shape to the IL guiding catheter (e.g. Judkins left guiding catheter) was not analyzed. These catheters could also be potentially useful in BPA.

Conclusion

The IL guiding catheter may be useful for BPA insertions in which it is difficult to advance a conventional guiding catheter into some vessel branches. This technique improves the safety of BPA.

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Disclosure

Conflicts of interest: None.

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