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ABSTRACT

Objectives Follow-up invasive coronary angiography (FUICA) after percutaneous coronary intervention (PCI) has been shown to increase the rate of early coronary revascularisation without reducing the incidence of subsequent myocardial infarction or death. However, no studies have evaluated the cost-effectiveness of FUICA in patients after coronary stenting. Therefore, this study aimed to evaluate the cost-effectiveness of FUICA after PCI.

Design Retrospective observational cohort study.

Participants and interventions Overall, 558 patients who underwent coronary artery stenting between April 2014 and March 2015 were matched and included in the invasive angiographic follow-up (AF) group (n=279), in which patients underwent FUICA 6–12 months after PCI, or in the clinical follow-up alone group (CF; n=279) using propensity scores.

Primary and secondary outcome measures The primary endpoint was the composite outcome of death, myocardial infarction, urgent coronary revascularisation, stroke or hospitalisation for the heart failure. The secondary endpoints included all-cause death, non-fatal myocardial infarction, urgent revascularisation, coronary artery bypass grafting, stroke, hospitalisation for the heart failure and any coronary revascularisation after a minimum of 6 months of follow-up.

Results Costs were calculated as direct medical expenses based on medical fee billing information. The cumulative 3-year incidence of the primary endpoint was 5.3% in the AF group and 4.7% in the CF group (HR 1.02; 95% CI 0.47 to 2.20; p=0.98). The total incremental cost at the 3-year endpoint in the AF group was US$1874 higher than that in the CF group (US$8947±US$5684 vs US$7073±US$6360; p≤0.001).

Conclusions FUICA increased the costs but did not improve clinical benefits. Thus, FUICA is not economically more attractive than CF alone.

Trial registration number UMIN000039768.

INTRODUCTION

Previous studies have shown that routine follow-up invasive coronary angiography (FUICA) after percutaneous coronary intervention (PCI) increases the rate of early coronary revascularisation without reducing the incidence of subsequent myocardial infarction or death. Current guidelines recommend a functional assessment to determine the clinical appropriateness of revascularisation to avoid unnecessary interventions and do not support the universal application of FUICA. The use of invasive coronary angiography decreased by approximately 30% in several US states between 2000 and 2009. Coronary angiography has been used to evaluate the performance of new technologies in the era of drug-eluting stents, whereas FUICA after PCI is commonly implemented to evaluate restenosis of the target lesions as the routine course of care in Japan. The Japanese Registry of All Cardiac and Vascular Diseases reported that the total number of annual coronary angiographies between 2015 and 2018 was flat at approximately 500 000. The definition of potential clinical benefits of FUICA and its selective use in high-risk
populations remain controversial, and the 2018 revision of the Japan Circulation Society guidelines suggests that routine coronary angiography after PCI is obsolete.11 12

The FAME 2 randomised trial compared a fractional flow reserve (FFR)-guided PCI strategy with medical therapy in patients with stable coronary artery diseases.13 PCI for lesions with reduced flow reserve has been shown to improve long-term clinical outcomes and become economically attractive.14 In recent years, coronary CT angiography has been increasingly used to evaluate patients with stable chest pain.15 When the prevalence of target or new coronary lesions decreases, FUICA is expected to have economic disadvantages.3 11 12 However, no studies have evaluated the cost-effectiveness of FUICA in patients after coronary stenting. Therefore, we investigated the relative cost and cost-effectiveness of adding angiography to the post-PCI management of coronary artery disease universally in real-world clinical practice in Japan.

METHODS

Study design and patient selection
This retrospective observational cohort study compared coronary angiography follow-up (AF) strategies after PCI with clinical follow-up (CF). The data source was the medical service database managed by a specialised public organisation (Social Insurance Medical Fee Payment Fund) in accordance with the format stipulated by the Japanese government’s Ministry of Health, Labour and Welfare (Notification: Vol. 0831 No. 1). From this data source, we used medical economic big data, which included medical service bills gathered from public insurers (including health insurance societies of companies) throughout Japan (The BD: The Tokyo University Health Economy Big Data). Data from 7 million insured patients were gathered. This database is updated every 6 months and is linked in chronological order using a management ID. During each annual update, the transfer of insured persons will be based on the prevailing exchange rate in April 2014 and March 2015 and collected clinical and cost data from 1 year before to 3 years after index PCI in chronologically linked participants with a uniform ID. Health insurance data of the patients who changed the insurance provider during the observation period were not included in the analysis. Further, patients who underwent PCI, coronary artery bypass grafting, or dialysis within 1 year before PCI were not enrolled. The exclusion criteria were as follows: concurrent end-stage renal failure on dialysis or cancer treated with surgery or chemotherapy during enrolment and/or follow-up.

This study was carried out in accordance with the RECORD statement. As we used a limited data set with personally identifiable information removed for analysis, the need for informed consent was waived (opt-out format). Owing to the sensitive nature of the data collected for this study, data that support the findings of this study are available from the operating officer on reasonable request.

This study was analysed from a social perspective. Cost indicators included reimbursement claims for medical services related to eligible diseases at medical institutions and pharmacies. The final medical and economic considerations were the cost-effectiveness and factors influencing the follow-up of AF and CF. The study aimed to evaluate the socioeconomic status of FUICA from a health insurance perspective.

Study endpoints and follow-up
The primary endpoint was the rate of major adverse cardiac events, defined as a composite of death from any cause, including nonfatal myocardial infarction, urgent coronary revascularisation, stroke or hospitalisation for heart failure. The secondary endpoints included all-cause death, nonfatal myocardial infarction, urgent revascularisation, coronary artery bypass grafting, stroke, hospitalisation for heart failure and any coronary revascularisation after a minimum of 6 months of follow-up. This report focuses on 3 years of clinical outcomes and cost-effectiveness.

Follow-up included FUICA 6–12 months after PCI, and coronary angiography performed thereafter. CT angiography cases were followed up for 6 months after PCI, and cardiac imaging with other modalities and physiologic studies performed clinically on an outpatient basis (ECG, stress ECG and echocardiography) were observed immediately after PCI until March 2018.

The cost indicators of this study were based on direct medical costs and those accounted for the cost of coronary angiography, cost of outpatient visits for clinical events directly related to cardiovascular disease (prescribing, dispensing, medication, medical instruction and patient education, and physiological and cardiac modality testing), and cost of treatment of endpoints (hospitalisation expenses, including pharmaceuticals, medical devices, laboratory tests and medical procedures) as CF costs. Outpatient costs not directly related to trauma, ophthalmology, otolaryngology and other procedures were excluded, and indirect medical costs, such as lost labour productivity, travel expenses, and patient and family welfare (care) costs, were also not included in the analysis. The conversion from Japanese Yen (JPY) to US Dollar (USD) was calculated based on the prevailing exchange rate in April 2014 (US$1=JPY102.5).

Statistical analysis
Categorical data were compared by using \( \chi^2 \) test or Fisher’s exact test, and sequential data were compared
Table 1  Baseline characteristics of the entire study population (prematch) and matched pairs (postmatch)

|                          | Prematch |           | Postmatch |           |
|--------------------------|----------|-----------|-----------|-----------|
|                          | AF group | CF group  | P value   | AF group  | CF group  |
|                          | n=371    | n=356     |           | n=279     | n=279     |
| Clinical characteristics  |          |           |           |           |           |
| Age, years                | 55.5±6.5 | 55.7±6.72 | 0.97      | 55.6±6.6  | 55.5±7.4  |
| Male                     | 329 (88.7) | 322 (90.4) | 0.44      | 249 (89.2) | 252 (90.3) |
| Prior myocardial infarction | 30 (8.1) | 41 (11.8) | 0.09      | 27 (9.3)  | 27 (9.3)  |
| Prior use of DAPT        | 47 (12.7) | 40 (11.2) | 0.55      | 27 (9.7)  | 31 (11.1) |
| Prior stroke              | 17 (4.6)  | 23 (6.5)  | 0.27      | 14 (5.0)  | 14 (5.0)  |
| History of heart failure  | 50 (13.5) | 42 (11.8) | 0.50      | 32 (11.5) | 36 (12.9) |
| Atrial fibrillation       | 12 (3.2)  | 7 (2.0)   | 0.28      | 7 (2.5)   | 6 (2.2)   |
| Peripheral artery disease | 43 (11.6) | 36 (10.1) | 0.52      | 26 (9.3)  | 26 (9.3)  |
| Acute myocardial infarction | 97 (26.1) | 68 (19.1) | 0.02      | 64 (22.9) | 61 (21.9) |
| Unstable angina           | 56 (15.1) | 60 (16.9) | 0.51      | 45 (16.1) | 43 (15.4) |
| Stable coronary artery disease | 218 (58.8) | 228 (64.0) | 0.14      | 170 (60.9) | 175 (62.7) |
| Angiographic and procedural characteristics |          |           |           |           |           |
| Numbers of stents used (per patient) | 1.6 | 1.67 | 0.36 | 1.59 | 1.59 |
| Drug-eluting stents use   | 345 (93.0) | 322 (90.4) | 0.21 | 255 (91.4) | 258 (92.5) |
| Bare-metal stents use     | 34 (9.3)  | 36 (10.0) | 0.74      | 32 (11.5) | 30 (10.8) |
| Minimum stent diameter, mm (IQR) | 3 (2.5–3.5) | 3 (2.5–3.5) | 0.90 | 3 (2.5–3.5) | 3 (2.5–3.5) |
| Total stent length, mm (IQR) | 29 (20–51) | 28 (20–52) | 0.83 | 29 (20–51) | 28 (20–50) |
| Fractional flow reserve   | 30 (8.1)  | 16 (4.5)  | 0.05      | 15 (5.4)  | 15 (5.4)  |
| Medications               |          |           |           |           |           |
| Aspirin                   | 348 (93.8) | 331 (93.0) | 0.66 | 257 (92.1) | 256 (91.8) |
| Thienopyridine            | 367 (98.9) | 354 (99.4) | 0.44 | 276 (98.9) | 277 (99.3) |
| Cilostazole               | 13 (3.5)  | 10 (2.8)  | 0.59      | 10 (3.6)  | 8 (2.9)   |
| Statins                   | 333 (89.8) | 307 (86.2) | 0.14 | 248 (88.4) | 241 (86.4) |
| ACE-I/ARB                 | 229 (61.7) | 214 (60.1) | 0.66 | 169 (60.6) | 171 (61.3) |
| Bata blockers             | 187 (50.4) | 168 (47.2) | 0.39 | 138 (49.5) | 137 (49.1) |
| Calcium-channel blocker   | 138 (37.2) | 147 (41.3) | 0.26 | 98 (35.1)  | 106 (38.0) |
| Insulin/oral hypoglycaemic agents | 114 (30.7) | 110 (30.9) | 0.96 | 89 (31.9)  | 90 (32.3)  |
| Direct oral anticoagulant | 5 (1.3)   | 5 (1.4)   | 0.95      | 4 (1.4)   | 3 (1.1)   |
| Warfarin                  | 15 (4.0)  | 16 (4.5)  | 0.76      | 11 (3.9)  | 13 (4.7)  |
| Proton pump inhibitor     | 290 (78.2) | 265 (74.4) | 0.24 | 213 (76.3) | 209 (74.9) |
| H2 blocker                | 25 (6.7)  | 39 (11.0) | 0.05      | 23 (8.2)  | 22 (7.9)  |
| Clinical follow-up        |          |           |           |           |           |
| Outpatient rehabilitation | 14 (3.8)  | 12 (3.4)  | 0.77      | 9 (3.2)   | 8 (2.9)   |
| ECG                       | 349 (95.1) | 342 (95.0) | 0.95 | 267 (95.7) | 263 (94.3) |
| Exercise stress test      | 131 (35.7) | 133 (36.9) | 0.73 | 103 (36.9) | 101 (36.2) |
| Echocardiography          | 263 (71.7) | 243 (67.5) | 0.22 | 192 (68.8) | 200 (71.7) |
| Coronary CT angiography   | 20 (5.4)  | 49 (13.8) | <0.001    | 18 (6.5)  | 28 (10.0) |
| Cardiac MR                | 6 (1.6)   | 5 (1.4)   | 0.81      | 5 (1.8)   | 2 (0.7)   |
| Cardiac nuclear scan      | 56 (15.1) | 38 (10.7) | 0.08      | 38 (13.6) | 34 (12.2) |

Values are expressed as mean±SD, n (%), or median (IQR). AF, angiographic follow-up; ARB, angiotensin receptor blocker; CF, clinical follow-up; DAPT, dual antiplatelet therapy; H2 blocker, histamine type-2 receptor blocker.
using the t-test or Mann-Whitney U test as needed. Categorical variables are expressed as numbers (%), and continuous variables are expressed as mean±SD or median of the IQR.

Propensity score (PS) was derived using a logistic regression model that included all baseline clinical characteristics, PCI, pharmacological characteristics, CF data and the size of the treatment centre. The discriminative power of periodic coronary angiography was confirmed based on the receiver operating characteristic curve. The corrected sample size for AF and CF groups was calculated using PSs.

The cumulative incidence of clinical events was assessed using the Kaplan-Meier method and compared using the log-rank test. Cox proportional-hazard models were fitted to estimate hazard ratios with 95% CIs for between-group comparisons. When no additional benefit for clinical outcomes could be determined between the AF and CF groups, a cost-minimisation analysis was performed to compare the cumulative costs of each group, and the incremental cost-effectiveness ratio was not calculated. Comparisons of the baseline and the 1-year, 2-year or 3-year cost indicators were made using paired t-tests, and comparisons of differences between groups were made using two-sample t-tests. All statistical analyses were performed using SPSS V.25.0 (IBM) software. All reported p-values were two sided, and p<0.05 was considered statistically significant.

**Patient and public involvement**

We used a medical service database, and hence, patients were not directly involved in this study.

- **RESULTS**

  **Baseline characteristics of all patients**

  A total of 856 patients from 497 hospitals who underwent coronary stenting between April 2014 and March 2015 were enrolled; 67 patients (7.8%) were lost to follow-up in 6 months. In addition, 6 patients with end-stage renal failure (0.7%) who received haemodialysis and 56 patients (6.5%) who received cancer treatment during enrolment and follow-up were excluded after enrolment. Overall, 727 patients were considered eligible, and their baseline characteristics are presented in table 1.

  **PS and matching**

  The discriminating power of the logistic regression model used to derive PSs was confirmed based on the area under the receiver operating characteristic curve (0.68). PS matching created 279 patient pairs in the AF and CF groups. The mean PS before matching was 0.562 (95% CI 0.545 to 0.577) for AF patients and 0.457 for CF patients (95% CI 0.442 to 0.472; p<0.0001). After matching, patients with AF had a mean PS of 0.506 (95% CI 0.491 to 0.522) and patients with CF had a mean PS of 0.497 (95% CI 0.482 to 0.513; p<0.431). The groups were well balanced (table 1). The average age of patients was 55.6 (SD 6.9) years, and 57 patients (10.2%) were women. CT angiography was performed in 3 and 15 patients 6–12 months after index PCI and 15 and 13 patients after 1 year in the AF and CF groups, respectively (table 1).
Clinical outcomes
The median follow-up time after index PCI was 31 (IQR: 27–32) months in the overall study population (32 (IQR: 27–36) months in the AF group and 32 (IQR: 27–37) months in the CF group; p=0.61). FUICA showed no clinical benefits, and the cumulative 3-year incidence of the primary endpoint (major adverse cardiac and cerebrovascular events) was 5.3% and 4.7% in the AF and CF groups, respectively (HR 1.02; 95% CI 0.47 to 2.20; log-rank p=0.98) (table 2, figure 1).

The 3-year cumulative incidence of all-cause death, myocardial infarction, urgent coronary revascularisation, coronary artery bypass grafting, stroke and hospitalisation for heart failure was not significantly different between the AF and CF groups. However, coronary revascularisation after 1 year of index PCI was performed more often in the CF group than in the AF group, and the cumulative 3-year coronary revascularisation incidence was 13.2% and 15.7% in the AF and CF groups, respectively (HR 1.35; 95% CI 0.85 to 2.14; log-rank p=0.23) (table 2, figure 2). These results were consistent with those of the previous studies conducted 1 year after PCI.

Cost outcomes
The initial FUICA cost was significantly greater in the AF group than in the CF group (US$1995±US$930 vs $0; p<0.001). During the follow-up, the AF group had significantly higher cumulative outpatient costs (US$791±US$464 vs US$697±US$490; p=0.02) and higher echocardiography costs (US$156±US$145 vs US$118±US$130; p=0.001) than that of the CF group. The 3-year cumulative average cost was significantly higher in the AF group than in the CF group due to differences in angiography costs (US$8947±US$5684 vs US$7073±US$6360; p<0.001) (table 3, figure 3).

The cumulative median costs were US$7614 (IQR US$5725–US$10423) for the AF group and US$5570 (IQR US$3386–US$8271) for the CF group.

Despite the relatively low cost of elective coronary revascularisation, the magnitude of difference between the cost of coronary angiography performed within 1 year and that after 3 years did not reduce (figure 3).

Cost minimisation analysis
Since no additional clinical benefit was identified in the AF group compared with the CF group, cost-effectiveness was assessed using cost-minimisation analysis. In this study, FUICA after PCI was inefficient, and the cost was as high as US$1873 over 3 years.

DISCUSSION
The primary finding of this study was that FUICA did not show any additional clinical benefit and was more expensive at the 3-year follow-up than the CF. Thus, FUICA is an economically unattractive strategy.

FUICA after PCI has been reported to increase the rate of early coronary revascularisation without a clear reduction in subsequent major adverse clinical events. In the randomised ReACT trial (Randomised Evaluation of Routine Follow-up Coronary Angiography After Percutaneous Coronary Intervention Trial) in Japan, the cumulative 5-year incidence of the primary endpoint of routine FUICA and CF was not significantly different (22.4% vs 24.7%; log-rank p=0.70). Consistently, no significant difference was observed between the AF and CF groups in the current study. In the AF group, 11 elective PCI procedures were performed within 3 months, suggesting the possibility of ad hoc PCI after angiography. However, the rate of coronary revascularisation increased with CF (14.3% vs 18.5%; log-rank p=0.077). Late progression of new or non-target lesions may explain why the trends in previous studies differ from those in the present real-world study. A higher rate of non-target lesion revascularisation (TLR) was observed in the late CF group in both the ReACT trial and a substudy of the SPRITIII (Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de novo Native Coronary Artery Lesions) trial. The use of...
of coronary CT angiography at follow-up of patients with established coronary artery disease, despite the strength of its morphological insights, is generally discouraged due to the lack of information related to functional ischaemia. The relative increase in non-TLR in post-PCI revascularisation may suggest that similar diagnostic management to basic assessment may be applicable in the future post-PCI follow-up of a chronic coronary syndrome.5

The FUICA was found to be economically disadvantageous in this study. In previous studies, the costs associated with this procedure were not investigated. Our study combined 3-year clinical and cost data. To our knowledge, this is the first economic analysis of FUICA after PCI. The FAME 2 trial compared an FFR-guided PCI strategy with medical therapy in patients with stable coronary artery disease.13 Medical therapy for lesions with reduced flow reserve was associated with increased follow-up costs with subsequent revascularisation and coronary angiography, and there was no significant difference between the average cumulative cost over 3 years and the higher cost of the initial PCI procedure.14 The FUICA strategy in this study did not reduce the magnitude of the mean cost difference of FUICA in the first year and the 3-year follow-up despite the lower costs of subsequent coronary revascularisation and coronary CT. In addition, the rate of coronary angiography after 1 year did not increase in the CF group.

The cost-effectiveness evaluation in this study may reinforce the clinical utility of evaluating FUICA in previous studies. All previous randomised controlled trials showed low event rates for primary endpoints, such as myocardial infarction and death, and did not detect the modest benefits or harms of FUICA.9 12 13 The value of economic analysis to investigate the cost implications of evidence-based clinical practice changes and to improve the efficiency of cardiac care has been emphasised in recent years.15 Therefore, it

| Table 3 Costs during the 3-year follow-up period |
|-----------------------------------------------|
| AF group (n=279) | CF group (n=279) | P value |
|------------------|-----------------|---------|
| Follow-up costs per capita, $                   |                   |         |
| Invasive coronary angiography                     | 1995±930          | 0±0     | <0.001  |
| 1-year prescribing, dispensing and medicines      | 3836±2625         | 3794±2455 | 0.843   |
| Antiplatelet medicines                            | 956±887           | 960±980  | 0.954   |
| Other medicines                                   | 869±1153          | 886±1054 | 0.857   |
| Outpatients visits                                | 791±464           | 697±490  | 0.021   |
| Coronary CT angiography (400)                     | 35±150            | 48±159   | 0.323   |
| Cardiac MR (378)                                  | 6±49              | 4±55     | 0.626   |
| Cardiac nuclear scan (801)                        | 159±535           | 103±337  | 0.140   |
| Electrocardiogram (32)                            | 92±101            | 82±88    | 0.214   |
| Exercise stress test (80)                         | 46±93             | 43±89    | 0.735   |
| Echocardiography (100)                            | 156±145           | 118±130  | 0.001   |
| Cardiac events                                   |                   |         |
| MACCE                                           | 496±3069          | 750±3982 | 0.400   |
| Stable revascularisation                          | 994±3153          | 1299±3530 | 0.282   |
| 3-y total costs per capita, $                     | 8947±5584         | 7073±6360 | <0.001  |

Values are expressed as mean±SD (mean inspection cost). The number of patients with ≥1 event was evaluated during the entire follow-up period; the cumulative cost was estimated at 3 years.

AF, angiographic follow-up; CF, clinical follow-up; MACCE, major adverse cardiac events.

Figure 3 Differences in costs mean cumulative medical costs (lines) at 1, 2 and 3 years and mean annual follow-up and events costs (bars) for the AF and CF groups up to 1 year, 1–2 years and 2–3 years after index PCI. Error bars and values in parentheses indicate 95% CIs. *Significant difference. AF, angiographic follow-up; CF, clinical follow-up alone; PCI, percutaneous coronary intervention.
is important to demonstrate the extent of the economic burden of FUICA. Most acute inpatient care services in Japan are reimbursed under the Diagnosis Procedure Combination/Per-Diem Payment System, a comprehensive daily evaluation system. The cost of surgery, including PCI and invasive angiography, is calculated based on fee-for-service payment model to arrive at the total cost. Major adverse cardiac event costs were calculated based on the hospitalisation costs for nonfatal myocardial infarction, emergency coronary revascularisation, stroke, heart failure and death events. In this study, the number of patients treated for MACCE was 13 in each group, and the small size with the 3-year cumulative event increased the SD of the mean costs of hospitalisation. The impact of event hospitalisation costs on cumulative costs was limited, but future widespread application of functional ischaemic assessment may reduce the differences in the cumulative costs. This study reflects daily clinical practice in Japan 4 years after the start of the ReACT study in 2010. The current study population included a higher proportion of youth with employer insurance, and the proportion of patients taking acute myocardial infarction drugs, antihypertensives, statins or antiplatelet drugs was consistent with that of the ReACT. In 2014, 200 142 coronary stents were performed in Japan, of which 52 872 (26%) were performed in patients aged 65 years or younger, according to the National Database of Health Insurance Claims and Specific Health Checkups of Japan. Because the same patient may receive treatment more than once, the expected nationwide number of patients will be smaller. In excluded patients with end-stage renal disease undergoing haemodialysis and those requiring cancer treatment, the risk of coronary angiographic invasions and associated complications are of greater concern, and the indications for FUICA should be carefully considered. Coronary angiography was performed in 51% of patients who underwent PCI in the data set, but the number of revascularisation procedures without additional evidence of functional ischaemia might have begun to decrease since the guidelines were revised based on the results of previous studies. The selective use of FUICA in high-risk populations and the detection of late adverse events after 1 year associated with target lesions remains challenging.

This study has some limitations. The clinical results of this study were similar to those of the previous Japanese studies in terms of all coronary revascularisation events. Although the primary endpoint had a lower event rate, the nature of the study data source raised concerns regarding missing events, and the sample size was not sufficient to determine the equivalence of AF strategies. All the patients who underwent invasive coronary angiography 6 to 12 months after PCI were included in the AF group, and the AF strategy may include patients who were not routinely indicated for angiography if analysed on a case-by-case basis. Therefore, if a future large study detects a modest benefit of FUICA, a different cost-effectiveness analysis will be required. The rates of the left main trunk, multivessel coronary artery disease, double stents, and renal and cardiac functions could not be identified in the medical claim information and therefore, were not analysed. The AF group had more cardio nuclear medicine tests performed in the pre-PS matching group than in the CF group. This could have created a bias in the health economics assessment, as patients undergoing FUICA might have been treated in hospitals with more resources. Finally, as the analysed costs are the actual direct medical expenses based on the Japanese medical fee system, generalising the results of this study to populations outside Japan should be done with caution.

CONCLUSION

The 3-year cost-effectiveness analysis showed that periodic FUICA was not economically attractive compared with CF because FUICA increased costs but did not improve clinical outcomes.

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Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by the Institutional review board of the University of Tokyo Hospital—screening no.: 2018167 N1. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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