



STUDY PROTOCOL

Functional outcomes and quality of life reported by adult patients undergoing elective hip, knee and shoulder arthroplasty (PaRIS-IOR)

Study acronym	PaRIS - IOR
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Protocol version	Vers 1.0 November 29, 2018
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Study design	Prospective cohort study
Type	Academic / non-profit, monocentric, national
Financing	Independent/autonomous funding

BACKGROUND

The World Health Organization (WHO) has recently defined patient centeredness as a fundamental characteristic for the quality of health care (1). Patient centeredness can be measured through the collection of functional outcomes and quality of life reported by patients, the so-called Patient-Reported Outcome Measures (PROMs). The Organization for Economic Cooperation and Development (OECD) has launched an initiative (called PaRIS Initiative) for the systematic collection of PROMs in patients undergoing elective hip and knee prosthetic arthroplasty 6 and 12 months after surgery (2). Such data is already routinely collected in several OECD member countries that have implemented implant registries (3). The IRCCS Rizzoli Orthopedic Institute (IOR) was selected as a pilot center for the launch of the initiative, whose purpose is to accelerate the adoption and reporting of validated, standardised, internationally-comparable patient-reported indicators, particularly within patient registries. IOR was selected as a pilot center for the launch of the program in Italy because the Institute hosts the Registry of Orthopedic Prosthetic Implantology (RIPO) since 1990 (4). Given that RIPO also includes shoulder implants, the same data will be collected also for patients undergoing shoulder replacement.

OBJECTIVES OF THE STUDY

- 1) To monitor and analyze functional outcomes and quality of life reported by patients undergoing elective hip, knee and shoulder arthroplasty performed at the IOR;
- 2) To identify predictive factors influencing the evolution of patients-reported outcome measures.

STUDY DESIGN

Prospective cohort study.

METHODS

Setting of the study

The study will be carried out at 6 operative units of the IOR (Orthopedic and Traumatological I Clinic, Orthopedic and Traumatological Clinic II, Orthopedic and

Traumatologic Clinic III, Reconstructive Orthopedic Surgery - Innovative Techniques / Revision surgery of hip prosthesis and new implant development, Surgery of the Shoulder and Elbow, Orthopedics-Traumatology and Prosthetic Surgery and of hip and knee replanting). For patients accessing through the “hospitalization-before-surgery” pathway, the enrollment will take place in the specific ambulatory in the month preceding the intervention. The remaining patients will be enrolled directly at the operative Units involved.

Participants

Inclusion criteria:

1. Males and females aged 18-95 years
2. Be on the list for an elective primary arthroplasty of hip, knee or shoulder
3. Availability to sign the informed consent

Exclusion criteria:

1. Severe cognitive impairment
2. To be listed for arthroplasty for musculoskeletal cancer
3. Not eligible for the surgical intervention

Procedures

The study consists of 3 phases:

1. **Baseline:** identification of eligible patients that the meet inclusion criteria. The evaluation will be performed in the pre-hospitalization ambulatory in the month preceding the intervention or in the ward at the time of hospitalization; in this phase it is planned also to:
 - present the study to the patients and collect the informed consents for study participation for the treatment of personal data
 - collect patients' authorization to be contacted by mail or by telephone for the follow-up.

- Administer and collect 2 questionnaires (EQ-5D for all subjects and the joint-specific questionnaire: hip, knee or shoulder).

The baseline includes two different ways of distributing and collecting questionnaires, based on the method of hospitalization:

- For patients in the “hospitalization-before-surgery” pathway (about 90% of the study population), RIPO personnel will go to the pre-admission ambulatory and will distribute and collect informed consents and questionnaires. Patient questionnaires administered to patient not eligible for intervention at a later stage will be destroyed.
- For patients not in the “hospitalization-before-surgery” pathway (about 10% of the population), the RIPO personnel will go directly to the operative units, after checking the day before the scheduled hospitalizations, and will distribute and collect informed consents and questionnaires.

The staff in charge of the distribution and collection of the questionnaires will put their data on the front page of the questionnaire and then they will be transformed into an identification code containing the initials of patients' name and surname followed by a progressive number. This code be used for data entry in the CRF and then to reconcile the patient record with RIPO unique pseudo-anonymized identification code.

2. **6 and 12 months follow up:** the RIPO staff will send a mail containing the same 2 questionnaires described in the baseline phase together with an accompanying letter with the instructions and a pre-paid envelope; the subject will be asked to resubmit the questionnaires. It will be also indicated how to receive direct support by contacting the IOR. In the event that patients - after receiving the package with the follow-up questionnaires - do not send them within 1 month, they will be directly contacted by telephone.
3. **Data collection and processing** will be performed by the RIPO staff and the methodological and statistical support of the biomedical research and health services unit of the University of Bologna.

Questionnaires

Four validated questionnaires will be used in the study. One questionnaire (Euro Quality 5 Dimensions, EQ-5D) for the general assessment of patient's health status will be administered to all the patients in the study (5). Three other joint-specific questionnaires will be administered to patients depending on the surgery procedure they will be undergoing. The joint-specific questionnaires are: Hip disability and Osteoarthritis Outcome Score - Short Form (HOOS-PS) for patients undergoing hip replacement (6); Knee injury and Osteoarthritis Outcome Score - Short Form (KOOS-PS) for patients undergoing knee replacement (7); the American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form (ASES), for patients undergoing shoulder implants. This last questionnaire will be administered in a modified version that does not include the assessments performed by the orthopedic surgeon (8).

ENDPOINTS

The outcomes of interest are functional outcomes and quality of life, measured through the total scores and the subscales of the administered questionnaires.

In particular, for the joint-specific functional scales the total score will be used, while for the EQ-5D the scores of the single dimensions will be used, together with a total VAS score on a 0-100 scale, that measures the overall health status.

The type of intervention will be used to stratify patients into three groups (hip, knee and shoulder).

The socio-demographic and clinical variables of interest, such as sex, age, comorbidity, and patient's clinical history, will be extracted from the clinical records and the data recorded in the RIPO.

SAMPLE SIZE

All patients hospitalized for elective hip, knee and shoulder prosthetic surgery at the 6 participating Operative Units will be included in the study. Based on the number of surgical procedures (i.e. implants) carried out in 2016, it is planned to recruit a total of 1700

patients, of which 1100 with hip replacement, 500 with knee replacement and 100 with shoulder replacement. A 10% rejection rate and a 40% follow-up loss are expected.

QUANTITATIVE VARIABLES

The quantitative variables of the study, which include the total scores of the scales and the subscales of the questionnaires, will be treated as such in the analyses and therefore not transformed.

STATISTICAL ANALYSES

Statistical analyses will be performed by the RIPO biostatistician in collaboration with the biostatistician of the methodological and statistical support unit for biomedical and on health services research of the Department of Biomedical and Neuromotor Sciences of the University of Bologna.

To analyze the evolution of the functional outcomes and quality of life of patients at 6 and 12 months from the surgery according to the type of intervention - and to identify predictive factors that influence this evolution - generalized estimation equations (GEE) and structural equation models (SEM) will be used. These techniques allow to obtain robust estimates even in the presence of missing data. We estimate an attrition rate of about 40% of cases, and non-compliance in resubmitting the questionnaires is hypothesized not to be linked to a systematic reason (for example the lower severity of patients). Therefore the missing data is to be considered completely random (MCAR).

Sensitivity analyses will be performed to assess whether the hypothesized mechanism of data loss at follow-up is supported by the data, or if alternative mechanisms need to be considered.

STUDY DURATION AND TIMELINE

The study will have an overall duration of 30 months and will be considered in any case completed 6 months after the recruitment target is achieved.

The study timeline is the following:

- Months 1-12: Selection and enrollment of the patients and database implementation.
- Months 6- 24: Follow up (6 and 12 months) and database implementation.

- Months 24-30: Analysis of data and dissemination of results.

The approval of the Ethics Committee will be considered as the start date of the study.

Study start date: 1/1/2019 (after approval by the Ethics Committee)

Enrollment start date: 1/1/2019

End date of study: 30/06/2021

CONSENT TO PARTICIPATE AND PRIVACY

Participation in the study is exclusively on a voluntary basis. Each subject will obtain detailed information regarding the nature and the procedures of the project and its purposes. All patients must sign a written consent before being included. Sensitive data will be processed according to the regulations in force by the study manager. Furthermore, participants can withdraw their consent to participate at any time, without any consequence.

The protection of personal information provided by the subjects will be in accordance with current legislation on the protection of personal data. In line with international data protection legislation, the following measures will be taken:

- The access to the database will be restricted to authorized persons;
- The paper material will be stored in dedicated lockable cabinets not accessible to unauthorized parties;
- The questionnaires and all paper data will also be archived in digital format at the medical technology laboratory with private access through a password.

ETHICAL PRINCIPLES

The study protocol and related documents will be sent before starting the study to the competent authorities and to the ethics committee for approval. The responsible investigator will ensure that the study is conducted in accordance with the Helsinki Declaration in its most up-to-date version (Fortaleza, October 2013), as well as with all national and international legislation applicable to clinical research.

The protocol has been written and the study will be conducted according to the principles of ICH-GCP (ref: <http://www.emea.eu.int/pdfs/human/ich/013595en.pdf>).

FINAL REPORT AND PUBLICATION OF RESULTS

The principal investigator agrees to produce a final report, to publish all the data collected as described in the protocol and is responsible for data integrity and to ensure that data are reported responsibly and consistently. The publication of data from the present study will take place independently of the results.

The transmission or dissemination of study results through scientific publications and / or public presentations will be based on anonymous data and on statistical processing.

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