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Brief report

# A new responder criterion (relative effect per patient (REPP) > 0.2) externally validated in a large total hip replacement multicenter cohort (EUROHIP)

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SUMMARY

*Objective:* To validate a new method to identify responders (relative effect per patient (REPP) >0.2) using the OMERACT-OARSI criteria as gold standard in a large multicentre sample.
*Method:* The REPP ([score before − after treatment]/score before treatment) was calculated for 845 patients of a large multicenter European cohort study for THR. The patients with a REPP >0.2 were defined as responders. The responder rate was compared to the gold standard (OMERACT-OARSI criteria) using receiver operator characteristic (ROC) curve analysis for sensitivity, specificity and percentage of appropriately classified patients.
*Results:* With the criterion REPP>0.2 85.4% of the patients were classified as responders, applying the OARSI-OMERACT criteria 85.7%. The new method had 98.8% sensitivity, 94.2% specificity and 98.1% of the patients were correctly classified compared to the gold standard.
*Conclusion:* The external validation showed a high sensitivity and also specificity of a new criterion to identify a responder compared to the gold standard method. It is simple and has no uncertainties due to a single classification criterion.


## Introduction

Total hip replacement (THR) is one of the most successful treatment procedures for patients with hip osteoarthritis; THR alleviates the symptoms (e.g., pain and stiffness) and degree of disability[1–4]. The success of THR can be measured as responder rate defined by Outcome Measures in Rheumatoid Arthritis Clinical Trials/Osteoarthritis Research Society International (OMERACT-OARSI) with patient reported outcome measurement tools (PROM's)[5–11]. The responder rate for a surgical treatment (e.g., THR) contains valuable information and is easy to understand either for patients and general practitioners, surgeons and medical care providers[12–14]. For example in the multicenter EUROHIP study the responder rate for THR was 85.4%, meaning that 6 out of 7 patients had a clinical improvement above the level of a minimally clinically important difference and one of 7 patients does not profit from THR (being a "non-responder")[12]. This information may be helpful either for decision making for the patients and for process amelioration for surgeons analyzing possible factors to become a responder or possible factors to become a "non-responder".

But the method to calculate the responder rate is complex because one main criterion or two out of three subcriterias regarding pain or function needed to be fulfilled[5]. An easier method simple to calculate would be helpful to overcome this limitation. In the validation study of the relative effect per patient (REPP) [Fig. 1]

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REPP = (pre-treatment score) minus (post-treatment score) / (pre-treatment score)

Example 1: pre-treatment score 48, post-treatment score 2;
REPP = 48-2/48 = 46/48 = 0.96 = **responder**
Example 2: pre-treatment score 25, post-treatment score 16;
REPP = 25-16/25 = 9/25 = 0.36 = **responder**
Example 3: pre-treatment score 13, post-treatment score 35;
REPP = 13-35/13 = -22/35 = -0.63 = **non-responder**

**Fig. 1.** REPP formula and calculating REPP scores: three examples.

the threshold was defined with 0.2, representing a change equal or larger than the minimal clinically important difference (MCID)[15]. Incidentally a high agreement was found between the patients with a REPP>0.2 (91%) and the responder rate using the set of OMERACT-OARSI criteria (92%)[15].

The aim of this study was to validate this finding externally in a highly generalizable sample of patients undergoing THR for primary OA in 12 European nations and to determine whether it identifies the same patients as responders using the OMERACT-OARSI method as the gold standard.

## Method

We included patients who were enrolled in the EUROHIP study and had complete PROMs from the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) follow-ups pre-THR and one year postoperatively for the patients with unilateral THR[4,12]. The EUROHIP study included 1327 patients who underwent primary THR at 20 European orthopedic centers in 12 nations. The study began by collecting data in January 2004 and concluded in December 2006. The inclusion criteria were having a diagnosis of hip OA, undergoing primary THR, and providing signed informed consent. The exclusion criteria were severe mental illness or dementia and patients who were unwilling/unable to participate. Each center was responsible for obtaining local ethical approval. The study protocol and data collection forms were designed in Bristol, UK and Ulm, Germany by the study principle investigators (Paul Dieppe, Klaus-Peter Günther and Karsten Dreinhöfer). The patient questionnaire was reviewed for acceptability in Bristol and modified accordingly before it was sent to Ulm for translation and distribution. Questionnaires were sent to each center for translation and were returned for editing before being printed and distributed with a set of instructions.

The WOMAC score was calculated including all 24 questions of three dimensions pain, stiffness and physical function on a scale 0 indicating no symptoms and 100 extreme symptoms.

### *Outcome*

We defined the patient outcome using the responder rate calculated with the REPP score (REPP>0.2) as new criterion and compared it to the rate using the OMERACT-OARSI criteria as gold standard.

#### *REPP score and responder criterion*

The REPP (pre treatment (tt) score − post tt score)/pre tt score) was calculated for each patient with the WOMAC score [Fig. 1]. Every patient with a REPP >0.2 was defined as responder[15].

#### *OMERACT-OARSI responder criteria*

The OMERACT-OARSI responder criteria (Pham *et al.*) indicate a substantial improvement in pain or function of ≥50% and an absolute change of ≥20. If the patient does not fulfill these criteria, improvement in ≥2 of the three following criteria is necessary: ≥20% improvement in pain and an absolute change of ≥10, ≥20% improvement in function and an absolute change of ≥10, ≥20% improvement in the patient's global assessment, and an absolute change of ≥10[5].

### *Statistical analysis*

Descriptive statistics were used to determine the score variability before and after THR, as well as the number of responders. Cross tabulation of both methods was conducted to assess the percentage of patients who were appropriately classified. Receiver operator characteristic (ROC) curve analysis was used to assess the sensitivity, specificity, and percentage of patients who were appropriately classified compared to the newly proposed method, using the OARSI as the gold standard. Stata 13.1 software (Stata Corp., College Station, TX, USA) was used for all statistical analyses.

## Results

All patients with complete outcome data from the preoperative and 12-month postoperative assessments ($n = 845$, comprising 63.7% of all included patients) were included. The average patient age was 65.7 years (range, 26–92 years).

The median WOMAC score of the patients before and after THR decreased from 58.3 to 15.6 ($P < 0.001$). The REPP-scores ranged from 1 to −1.5, peaking at approximately 1 and slowly decreasing to zero; there were few results near or below zero, as well as an outlier. For the EUROHIP cohort, the relative proportions of responders were 85.4% and 14.6% non-responders (12.7% unchanged, and 1.9% worse). Using the OARSI-OMERACT criteria, we identified 85.7% of the patients as responders.

Both methods classified nearly the same patients as responders with 98.8% sensitivity, 94.2% specificity and 98.1% correctly classified, demonstrating good validation of the new REPP method to calculate the responders [Fig. 2].

## Discussion

### *Main findings*

The criterion REPP>0.2 to define a responder correlates with high sensitivity and also high specifity with the existing set of OARSI-OMERACT criteria. The responder rate can be calculated simple and easier with REPP method.

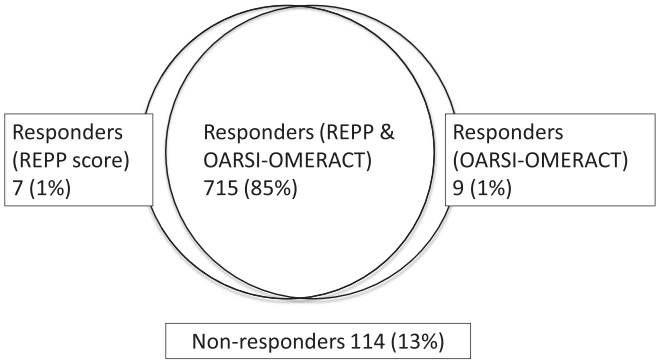


**Fig. 2.** Venn-diagram to show overleap between REPP score and OARSI-OMERACT responder criteria.

*Strengths/limitations*

The strength of this study is the large number of participating patients in 12 nations with PROM's in 10 different languages at 20 centers allowing a reliable external validation of this new method.

Study limitations were the selection bias of patients and treatment.

The included patients (unilateral osteoarthritis of the hip, undergoing THR) were similar to those in the validation study.

A basic bias of the EUROHIP study group was that all participating surgeons and centers had a special interest in THR and in clinical science; therefore, the analyzed cohort may represent a positive patient selection and the responder rate may be higher than in general practice.

## Author contributions

All authors have contributed to each of the three activities:

1) The concept of the REPP and the application of the new responder criterion the EUROHIP study cohort and the data acquisition of the cohort especially for the clinical part measuring the outcome
2) Drafting the article or revising it critically for important intellectual content
3) Approval of the final version, and will take public responsibility for the content of the paper.

## Role of the funding source

None.

## Competing interests

None.

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