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Attitudes and considerations of patients with ST-elevation myocardial infarction towards participation in randomized clinical trials

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Abbreviations: PCI, percutaneous coronary intervention; RCT, randomized clinical trial; STEMI, ST-elevation myocardial infarction.

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Abstract

Background: Limited evidence is available on attitudes and considerations of ST-elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (PCI) towards participation in randomized clinical trials (RCTs). Therefore, we investigated the ability of these patients to decide participation in RCTs.

Methods: This was a questionnaire-based study. Over a 9-month period, we approached and invited 100 consecutive STEMI patients who were asked to participate in at least one RCT during primary PCI. Patients were asked to fill out self-administered questionnaires concerning demographic data as well as attitudes and considerations towards participation in RCTs.

Results: Patients had a mean age (SD) of 61 (12) years and most were males (82%). With a response rate of 96%, a total of 94% accepted participation in at least one RCT. Most patients (78%) claimed to understand the information on participation in RCTs at an acceptable to satisfactory level, and 83% felt that they were given the possibility to ask additional questions during the decision-making process. Few patients (2%) claimed that they felt pressured to participate. The majority of patients (83%) stated that they participated to help clinical research, and 85% of patients would be willing to participate in future RCTs. It did not appear that the total number of RCTs in which patients participated in was of significant importance.

Conclusions: Patients with STEMI undergoing primary PCI had positive attitudes and considerations towards participation in RCTs despite their acute medical condition and the emergency environment. The overall self-assessed ability of patients to make a decision about participation in RCTs was good.

Keywords: Attitudes; Considerations; Ethics; Patient participation; Percutaneous coronary intervention; Randomized controlled trial; ST-elevation myocardial infarction.

Introduction

Randomized controlled trials (RCTs) remain the gold standard by which studies of treatment are assessed, and owing to several RCTs within the field of ST-elevation myocardial infarction (STEMI) research, the dominant reperfusion strategy has been deemed primary percutaneous coronary intervention (PCI), which has both improved survival and life quality of patients.(1) However, with demanding challenges in clinical practice such as improving access to care, door-to-balloon time, and adherence to guideline treatment recommendations, RCTs need to be even more sufficient in terms of developing novel treatments and improving existing ones for managing STEMI patients undergoing primary PCI.(2) As such, RCTs require efficient recruitment of adequately sized study populations being representative of contemporary clinical practice to be successful.(3) However, patient recruitment remains a widespread challenge across RCTs, and controversy over especially informed consent in STEMI RCTs has existed for more than 30 years.(4)

Although it is standard practice to ask STEMI patients to consent to participation in RCTs, this activity poses an ethical pitfall due to the acute medical condition of patients, the emergency environment, and the fact that randomization must occur within minutes of arrival at the catheterization laboratory.(4) Therefore, only limited time is remaining for oral and written information, and for patients to consider participation in RCTs. In addition, the psychological distress including fear of dying, ongoing pain, and helplessness associated with STEMI may compromise the decision-making process of patients and consequently the fundamentals of securing informed consent.(5) Currently, few studies have assessed attitudes and considerations of patients towards participation in RCTs during the acute phase of STEMI and primary PCI, thus deeper insight into this issue is warranted. Most of the focus in the literature has been on the experience of STEMI patients with the informed consent process in RCTs, although this may overlap with attitudes and considerations of patients in some of the studies.(6-17)

For these reasons, we investigated how STEMI patients undergoing primary PCI assessed their ability to decide participation in RCTs. We hypothesized that patients felt pressured to participate and had difficulty accepting participation if asked to enter more than one RCT.

Methods

Study design and setting

This was a questionnaire-based study conducted at the Department of Cardiology at Aalborg University Hospital, a tertiary referral hospital in the North Denmark Region, from March, 2012, to November, 2012. During this study period, our department had four running RCTs including *DANAMI-3*,(18) *SORT OUT VI*,(19) *MITOCARE*,(20) and *GEVAMI*,(21) in which participation could potentially be asked.

Study population

Our study population consisted of consecutive patients admitted with STEMI undergoing primary PCI who were asked to participate in at least one RCT. We only included patients ≥18 years of age who could read and understand Danish as these inclusion criteria were required by all RCTs.

Recruitment and sample size estimate

During the 9-month study period, trained research nurses (authors PB, AHA, MB, and HPH) approached patients. We asked 100 patients to participate in our study, which was needed to reach our sample size requirement of at least 80 respondents. This sample size estimate was calculated using Raosoft® sample size calculator with a 95% confidence interval and a 5% error margin.

Data collection

Data were collected using a self-administered questionnaire. A pilot study of 10 patients was conducted to assess whether any questions required revision, and this was not necessary.

Questionnaires were distributed to patients 6–48 hours following primary PCI. This ensured that patients were still in-hospital and had as well participation in RCTs as the provided information on RCTs present in memory.

The questionnaire was divided into two sections. Section 1 included age, sex, agreement for participation in RCTs, and the number of RCTs in which patients participated in. Section 2 assessed the following: level of understanding the actual RCT, level of opportunity to ask additional questions following the provided information, level of feeling pressured to participate, reasons for participation, and thoughts on future participation.

Some of the questions were closed-ended questions meaning that patients could only answer 'Yes', 'No', or 'Do not know.' Other questions were open-ended meaning that they could be answered on a scale ranging from 0–15 to give patients the opportunity of rating their experience.

Patients were anonymized and given a unique ID number for registration purposes during data collection and analysis.

Statistical analysis

Continuous variables were reported as mean (SD), and categorical variables as counts (%).

First, we stratified patients according to who accepted participation in RCTs, who did not accept participation, and who did not respond to the questionnaire. Between these groups, we tested for differences in age and sex as well as time, day, and month of admission with STEMI using independent t- and chi-squared tests, as appropriate. A p-value <0.05 was considered statistically significant.

Second, we collapsed questions based on the 0–15 scale into two groups, with scores between 0–5 indicating 'unacceptable level' and 6–15 indicating 'acceptable to satisfactory level.'

Data management and analysis were performed using Stata, version 15.0 (StataCorp, College Station, Texas, USA) and R, version 3.5.1 (R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: https://www.R-project.org/).

Ethics

The North Denmark Region Committee on Health Research Ethics was approached, and our study did not require approval according to the Danish Law of Questionnaires and Interviews. As our study hold no personal data, registration by the Danish Data Protection Agency was not required. Our study conforms to principles outlined by the Declaration of Helsinki,(22) thus our study was explained in written and oral format to patients. By Danish law, this type of questionnaire-based studies did not require informed consent of patients.

Sources of funding

No extramural funding was used to support this work. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper and its final contents.

Results

Patients and characteristics

Of all 100 consecutive STEMI patients undergoing primary PCI who were approached and asked to fill out the questionnaire in our study, 82 patients (82%) were males, and the remaining 18 patients (18%) were females. The mean (SD) age of patients was 61 (12) years. Most patients were asked to participate in RCTs during daytime hours and weekdays.

Participation

A total of 96 patients (out of 100) answered the questionnaire yielding a response rate of 96%. However, not all patients answered all questions resulting in varying response rates across individual questions.

While 94 patients (out of 100) (94%) accepted inclusion in at least one RCT, 6 patients (out of 100) (6%) declined participation. Overall, between the 90 patients participating, 6 not participating, and 4 not responding to the questionnaire, no differences in age (p=0.481) and sex (p=0.399) as well as time (p=0.531), day

(p=0.738), and month (p=0.617) of admission with STEMI were observed. A consort diagram of all participating, non-participating, and non-responding patients including their baseline characteristics is depicted in Figure 1. In addition, the distribution of patients across individual RCTs is depicted in Figure 2.

When comparing patients' perception of number of RCTs in which they participated in with the actual registered number of RCTs, most patients believed they participated in less RCTs than was actually the case, as depicted in Figure 3. In addition, 20 patients (out of 100) (20%) claimed they did not know in which RCTs they participated in.

Level of understanding

Patients were asked to rate their level of understanding the information provided on participation in RCTs using the 0–15 scale, as depicted in Figure 4. A total of 88 patients (out of 96) answered the question, and 69 patients (out of 88) (78%) claimed to understand the information at an acceptable to satisfactory level (score: 6–15, mean score: 11). In comparison, 19 patients (out of 88) (22%) rated their level of understanding at an unacceptable level (score: 0–5, mean score: 2).

Of the 6 patients declining participation in any RCT, 1 patient did not answer, 3 patients rated their understanding at an unacceptable level (score: 0–5), and the remaining 2 patients rated their understanding at an acceptable to satisfactory level (score: 6–15).

Additional questions

Patients were asked to rate their level of opportunity to ask additional questions about participation in RCTs using the 0–15 scale. A total of 84 patients (out of 96) answered the question, and 70 patients (out of 84) (83%) rated their experience at an acceptable to satisfactory level (score: 6–15), and 14 patients (out of 84) (17%) at an unacceptable level (score: 0–5).

Feeling pressured

Patients were asked to rate their level of feeling pressured to participate in RCTs, and how this affected their decision-making process using the 0–15 scale. Overall, 2 patients (out of 96) (2%) claimed to have felt pressured, of which 1 patient refrained from rating how this affected the decision-making process, and the remaining patient rated 8 meaning that this did not affect the decision.

A total of 94 patients (out of 96) (98%) stated that they did not feel pressured to participate in RCTs. Of these, 55 patients chose to rate their level and rated their experience between 7–15, with the majority (n=51) rating higher than 11.

Reasons for (non-)participation

Patients were asked to state one or more motivational factors for participation in RCTs, as depicted in Figure 5. The major reason for participation was 'To help clinical research,' which 75 patients (out of 90) (83%) marked.

The 6 patients declining participation in RCTs marked the following: 'Concerned about receiving an untested treatment' (n=1), 'Do not wish to participate' (n=1), 'Unable to manage the decision' (n=3), 'Wish to discuss participation with relatives' (n=1), 'Previous experience with clinical research' (n=1), 'Felt pressured to participate' (n=0), and 'Do not know' (n=2).

Future participation

Patients were asked if they felt positive about future participation in RCTs. A total of 93 patients (out of 100) marked: 'Yes' (n=79, 85%), 'No' (n=3, 3%), and 'Do not know' (n=11, 12%). Of these, the 6 patients declining participation in RCTs marked: 'Yes' (n=4), 'No' (n=1), and 'Do not know' (n=1).

Discussion

Our study revealed several valuable insights into attitudes and considerations of patients towards participation in RCTs during primary PCI for STEMI in Denmark. Our main finding was that 78% of patients showed an acceptable to satisfactory level of understanding the information provided on participation in RCTs, although only half correctly stated the actual registered number of RCTs in which they participated in. Further, patients did not feel pressured to participate and had the opportunity to ask additional questions during the decision-making process. Notably, most patients participated to help clinical research and were positive about future participation in RCTs.

To our knowledge, only limited evidence is available on attitudes and considerations of STEMI patients undergoing primary PCI towards participation in RCTs. Instead, most studies have focused on how STEMI patients understand the informed consent process in RCTs.(6-17) However, that selected Danish STEMI patients undergoing primary PCI in our study claimed they (a) had an acceptable to satisfactory level of understanding; (b) had the opportunity to ask additional questions; (c) did not feel pressured to participate; (d) wanted to help clinical research; and (e) were positive about future participation are all relevant findings underscoring the ethical justification of RCTs among STEMI patients.(4) These findings generally corroborates a recent international survey observing that out of 2,194 former clinical research participants nearly 50% participated to help advance clinical research, 81% considered the informed consent form easy to understand, and most would participate again and would recommend participation to others.(23) Studies have further suggested that STEMI patients participating in RCTs compared with similar non-participating patients overall had the same outcomes meaning that it is safe for STEMI patients to consent to RCTs without jeopardizing survival.(24, 25) Taken together, this further speaks to enhancing patient recruitment in STEMI RCTs as under-participation remains a longstanding systemic challenge worldwide.(3)

Significant determinants of understanding the information provided on participation in RCTs among STEMI patients have been found to be the absence of pain at inclusion, high educational level, and male sex.(13) Especially, pain and other symptoms experienced during STEMI have been found to explain why some patients consent to RCTs to rid themselves of pain and to receive treatment immediately.(4, 8, 10, 11,

16, 17) Our study revealed that the circumstances during primary PCI place high demands to physicians providing the information on RCTs, and how the specialized medical and nursing staff managing the patient during the emergency acts. As such, it remains crucial that patients understand and feel that participation in RCTs is completely voluntary.

Given the psychological distress of patients during the acute phase of STEMI and primary PCI, it is a challenge for physicians to thoroughly inform patients about RCTs. According to Ågård *et al.*, 86% of physicians felt that STEMI patients were unable to understand all the information provided on participation in RCTs.(7) However, in our study of selected STEMI patients undergoing primary PCI in Denmark, most patients (78%) claimed to understand the information at an acceptable to satisfactory level. Taken together, this was interpreted as sufficient as patients simultaneously felt they had the opportunity to ask additional questions during the decision-making process. In previous studies, rates of understanding the information provided on RCTs to make a good decision have been reported to range from 52–88%.(6, 9, 10, 12-17) In contrast, the corresponding rate in non-emergency cardiovascular RCTs has been reported to be as high as 90%.(26)

That only 2% of patients in our study claimed to have felt pressured to participate in RCTs during the acute phase of STEMI and primary PCI did not match our hypothesis, as we initially believed that most patients would feel obliged to participate. Accordingly, this is rather reflected by the fact that 83% of patients in our study participated to help clinical research, and 85% would be willing to participate in future RCTs. These response rates are generally comparable with those of previous studies.(9, 10, 12, 15, 16) In addition, as none of the patients commented on the number of RCTs in which they participated in, it did not appear that this was of significant importance to patients.

Despite promising, our findings should be considered in the light of various limitations. The findings may have been different in other countries due to cultural and social differences. The varying response rates across individual questions may raise the possibility of selection bias, as it is likely that returned questionnaires were from patients with more extreme experiences, both favorable and otherwise, or those interested in clinical research. Our study was conducted among STEMI patients asked to be included in at least one RCT during primary PCI, and it is possible that the study staff screened only patients they felt would accept participation rather than all patients meeting RCT criteria. In addition, the findings may be different in stud-

ies involving more chronic and stable patients who are usually outpatients and may consider participation in RCTs over days to weeks rather than minutes as STEMI patients have to.

Conclusion

Danish STEMI patients appeared to have positive attitudes and considerations towards participation in RCTs despite their acute medical condition and the emergency environment. The overall self-assessed ability of patients to make a decision about participation in RCTs was good, not influenced by pressure or misunderstanding of information, and driven by the fact that patients wanted to help clinical research and would be willing to participate in future RCTs.

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Conflicts of interest: All authors have no conflicts of interest in relation to the present topic.

Figure legends

Figure 1: Consort diagram of all participating, non-participating, and non-responding patients including their baseline characteristics.

Figure 2: The distribution of patients across individual RCTs.

Figure 3: Comparison of patients' perception of number of RCTs in which they participated in with the actual registered number of RCTs.

Figure 4: The rated level of understanding the information about participation in RCTs of patients using the 0–15 scale.

Figure 5: Motivational factors of patients towards participation in RCTs.

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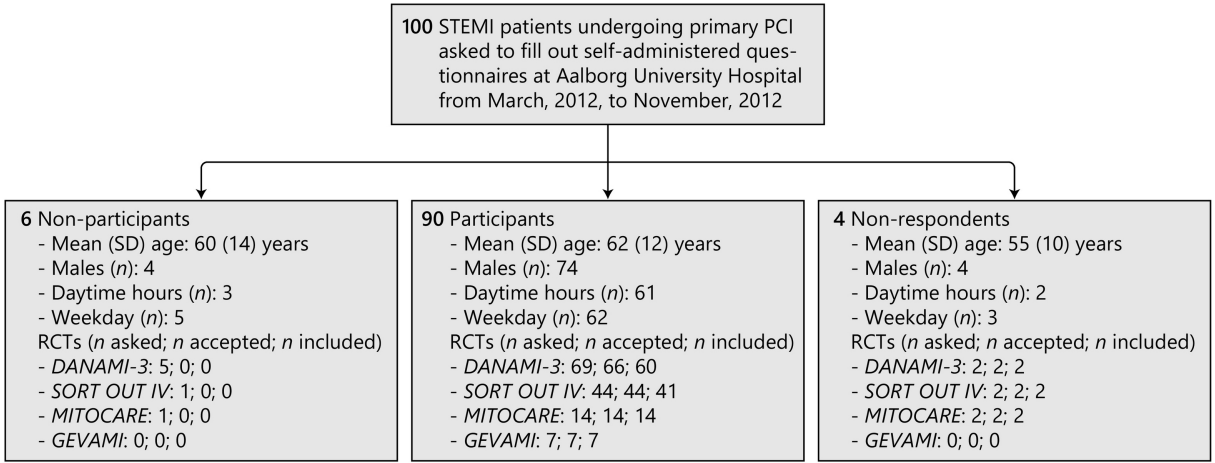
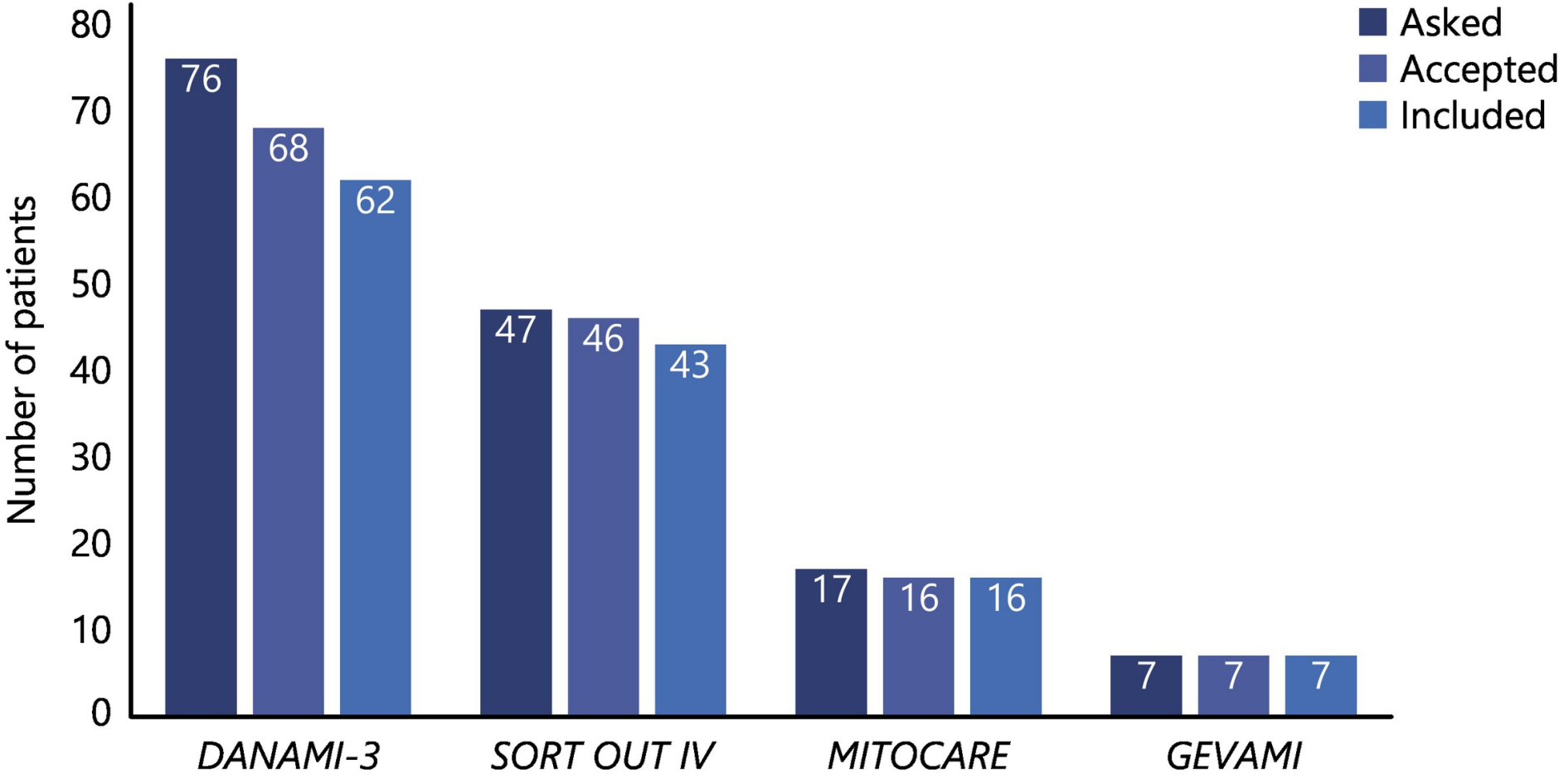

100 STEMI patients undergoing primary PCI asked to fill out self-administered questionnaires at Aalborg University Hospital from March, 2012, to November, 2012
6 Non-participants
- Mean (SD) age: 60 (14) years
- Males (*n*): 4
- Daytime hours (*n*): 3
- Weekday (*n*): 5
RCTs (*n* asked; *n* accepted; *n* included)
- *DANAMI-3*: 5; 0; 0
- *SORT OUT IV*: 1; 0; 0
- *MITOCARE*: 1; 0; 0
- *GEVAMI*: 0; 0; 0
90 Participants
- Mean (SD) age: 62 (12) years
- Males (*n*): 74
- Daytime hours (*n*): 61
- Weekday (*n*): 62
RCTs (*n* asked; *n* accepted; *n* included)
- *DANAMI-3*: 69; 66; 60
- *SORT OUT IV*: 44; 44; 41
- *MITOCARE*: 14; 14; 14
- *GEVAMI*: 7; 7; 7
4 Non-respondents
- Mean (SD) age: 55 (10) years
- Males (*n*): 4
- Daytime hours (*n*): 2
- Weekday (*n*): 3
RCTs (*n* asked; *n* accepted; *n* included)
- *DANAMI-3*: 2; 2; 2
- *SORT OUT IV*: 2; 2; 2
- *MITOCARE*: 2; 2; 2
- *GEVAMI*: 0; 0; 0

Figure 1


Asked
Accepted
Included
Number of patients
80
70
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40
30
20
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0
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7
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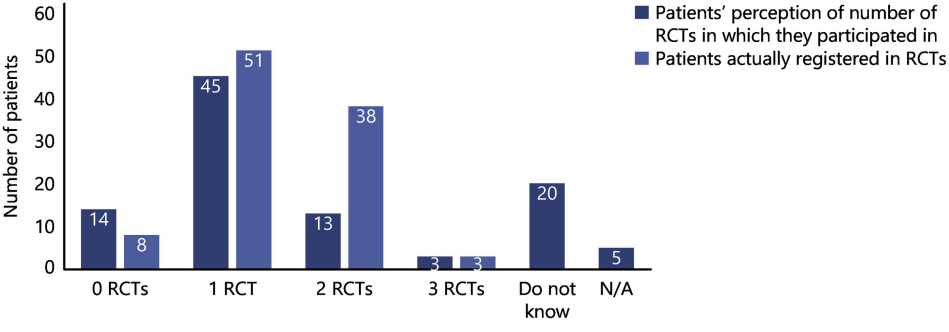
DANAMI-3
SORT OUT IV
MITOCARE
GEVAMI

Figure 2


Number of patients
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50
40
30
20
10
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Patients' perception of number of RCTs in which they participated in
Patients actually registered in RCTs
14
8
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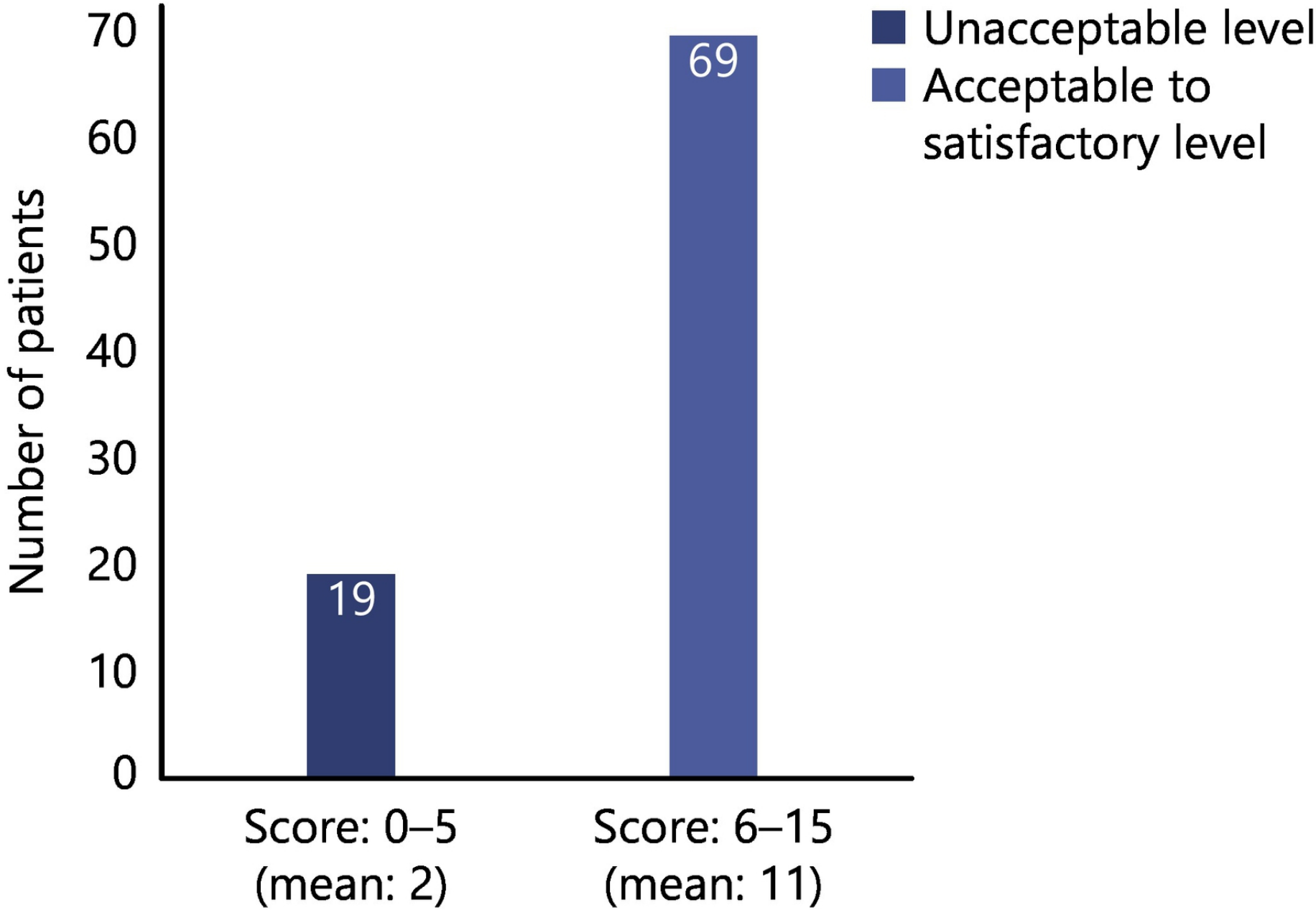
38
3
3
20
5
0 RCTs
1 RCT
2 RCTs
3 RCTs
Do not know
N/A

Figure 3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20
10
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Number of patients
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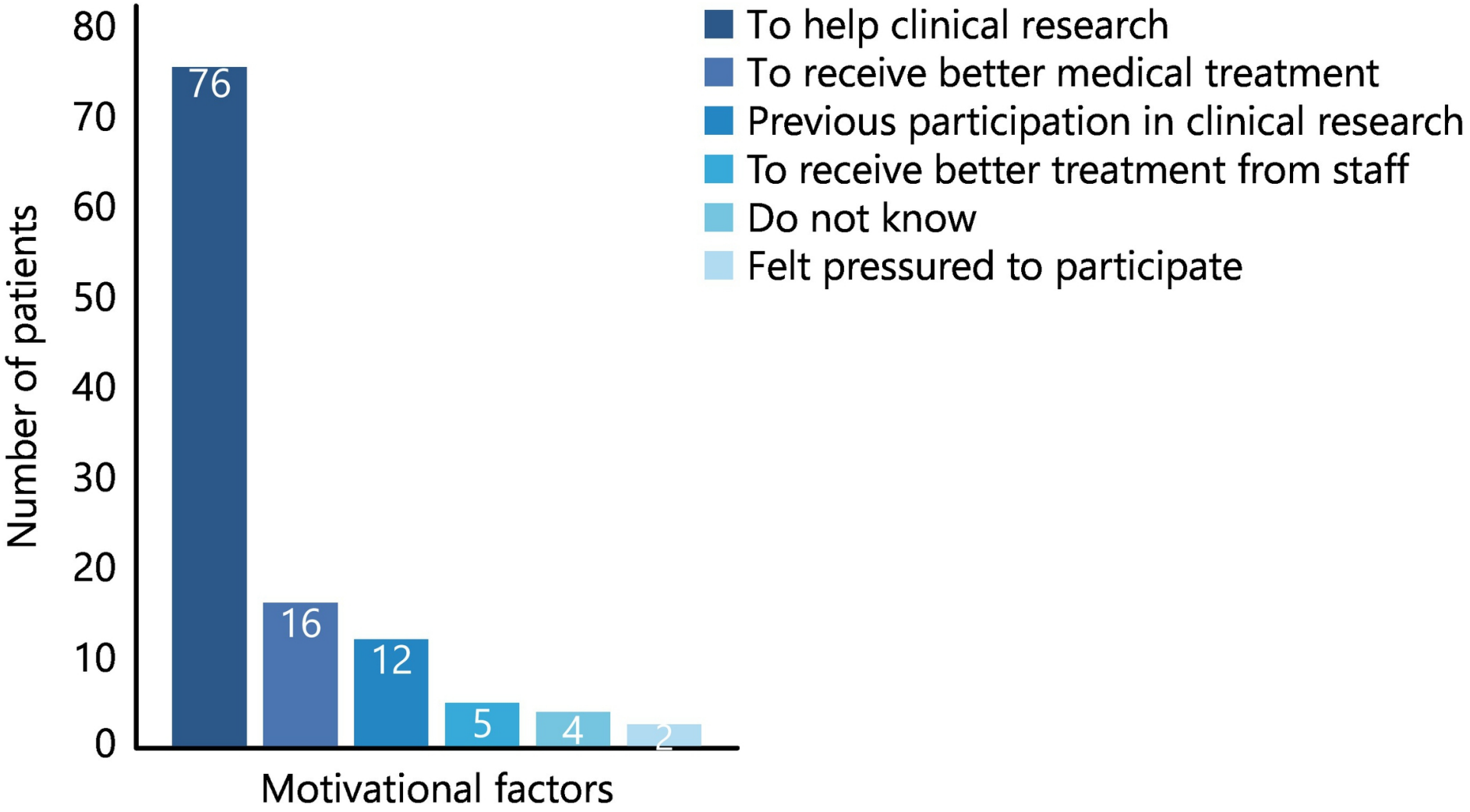
Unacceptable level
Acceptable to satisfactory level
Score: 0–5 (mean: 2)
Score: 6–15 (mean: 11)

Figure 4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Number of patients
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5
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Motivational factors
To help clinical research
To receive better medical treatment
Previous participation in clinical research
To receive better treatment from staff
Do not know
Felt pressured to participate

Figure 5