CARDIOVASCULAR MEDICINE

Patients' perceptions of informed consent in acute myocardial infarction research: a questionnaire based survey of the consent process in the DANAMI-2 trial

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Objective: To analyse how patients in the acute phase of a myocardial infarct experience the informed consent procedure of a clinical trial.
Design: A questionnaire based follow up survey including patients who gave informed consent as well as patients who did not consent to the trial.
Patients: 103 patients who gave informed consent and 78 who did not consent to the second Danish acute myocardial infarction trial (DANAMI-2).
Results: 76% of the trial participants and 63% of the non-participants agreed or mostly agreed that they felt able to make a decision about whether or not to participate in the trial; 50% of the trial participants and 34% of the non-participants found it acceptable that patients in their situation have to make such a decision. Only 28% of the trial participants and 7% of the non-participants read the information sheet before they made the decision.
Conclusions: Informed consent should be sought in acute myocardial infarction trials despite the emergency situation and the medical condition of the patients. Patients' self assessed ability to make a decision should be explicitly addressed during the informed consent process and patients should not be pressurised into decision making. Physicians and research ethics committees should focus specifically on improving the oral information.

The basic requirements of informed consent are that patients understand the information, that they are competent to make a decision, and that they arrive at their decision without being coerced or manipulated by the medical staff or others.[1] Seeking informed consent for clinical research from patients suffering acute myocardial infarction (AMI) is, however, an ethical challenge owing to the medical condition of the patients, the emergency situation, and the limited time available. There is no obvious solution to the particular difficulties of informed consent in this situation, and so patients have been enrolled in AMI trials on the basis of more or less comprehensive consent procedures.[2] Little is known, however, about how patients perceive the various enrolment procedures used in such trials. Empirical studies of the informed consent process in AMI trials have shown that consent obtained under these circumstances is not likely to be well informed.[3–9] Ågård and colleagues maintain that most of the patients in their study "were willing to allow, or even wanted, their physicians to decide for them—at least if they were to be too ill to be asked about participation in research".[8] None of the other studies, however, analyse whether patients find the consent procedure acceptable, and it remains an open question whether or not patients with AMI do in fact feel too ill to be asked about participation in research.

Using a questionnaire based follow up survey of patients who had to decide whether or not they wished to participate in a recent AMI trial—the DANAMI-2 trial (see the box)[10]—we addressed the ethical implications of patients' experiences with the informed consent process. It was our aim to analyse the extent to which the patients, both trial participants and non-participants, felt capable of making the decision, and whether or not they found the informed consent process acceptable. On the basis of these considerations, we discuss how the enrolment procedure of AMI trials may be improved.

METHODS

Two questionnaires (A and B) were developed on the basis of a qualitative interview study with patients who were informed about the DANAMI-2 trial (qualitative data reported elsewhere).[11] One questionnaire (A) was designed for patients who had participated in the DANAMI-2 trial, while the other (B) was designed for those patients who did not wish to participate or who were not able to give consent.

The questionnaires were developed on the basis of questions inspired by the interview study as well as by published reports on informed consent. The provisional questionnaires were mailed to 10 patients. Each item was subsequently discussed thoroughly with these patients to ensure that the items were understandable, unambiguous, and relevant, and the questionnaires were revised accordingly. This process of pilot testing was undertaken twice, and the final questionnaires—consisting of 46 items (questionnaire A) and 42 items (questionnaire B)—addressed patients' understanding of the information at the time of the consent, their self assessed ability to decide whether or not to participate, the reasons for their decision, and their overall response to the consent process.

The survey was made as a questionnaire based follow up study. Questionnaire A was mailed to 125 consecutive patients who did participate in the DANAMI-2 trial three weeks after the informed consent process. In all, 103 completed questionnaires were returned (response rate 82%) and the mean (SD) time from the consent process to the return of the questionnaires was 29.6 (5.2) days. Questionnaire B was mailed to 122 consecutive patients who did not participate in the DANAMI-2 trial; 78 completed

Abbreviations: AMI, acute myocardial infarction; DANAMI-2, second Danish acute myocardial infarction trial; HERO-2, Hirulog and early reperfusion or occlusion trial

Design of the DANAMI-2 trial

The DANAMI-2 trial (the second Danish acute myocardial infarction trial) was a randomised clinical multicentre trial comparing an interventional approach (primary angioplasty) with a medical strategy (fibrinolysis) in the treatment of acute myocardial infarction.[10] The primary angioplasty was done in only five (the angioplasty centres) of the 29 participating hospitals. Patients admitted to the remaining 24 hospitals (the referral hospitals) were randomised to immediate treatment with fibrinolytic therapy in the local hospital or acute ambulance transfer to an angioplasty centre for primary angioplasty. In all, 1572 patients participated in the trial (443 were randomised in the angioplasty centres and 1129 in the referral hospitals), while 505 eligible patients did not participate because they did not give informed consent. The study had its own independent safety and ethics committee which monitored the study and was responsible for producing an interim analysis.

In accordance with Danish legislation, patients were informed about the trial both orally and in writing (on a one page sheet) before they signed the consent form. As patients with a myocardial infarct need immediate medical attention, physicians had only a short period of time (less than 20 minutes) in which to decide whether the patient was eligible, inform the patient, obtain consent from the patient, randomise, and initiate the treatment. To help physicians with the informed consent process, The DANAMI-2 study group produced, in print, an outline of the oral information and some coloured illustrations of the heart and the two treatments.

questionnaires were returned (response rate 64%). Data on the time from the consent process to the return of the questionnaires were not available.

Five patients had died since the consent process and four were not eligible, as they participated in the qualitative interview study. Questionnaires A and B were analysed separately using SPSS 9.0 standard statistical tests of frequency distribution. Association tests (γ and χ^2) were used to analyse associations between variables. The study was approved by the regional research ethics committee (1999/4643).

RESULTS

Patient population

Table 1 describes the patient population who received the questionnaires. The non-responding trial participants were on average eight years older than participants who returned the questionnaire. No differences in sex, treatment (primary angioplasty or fibrinolysis), or hospital (referral or angioplasty centre) were found between respondents and non-respondents.

Information

Table 2 shows the extent to which the patients recalled being informed about the various elements of the trial. Non-participants were generally able to recall less of the information or were less well informed than the trial participants. In all, 59% of the trial participants were satisfied with the information, 4% found that they received too much information, 18% found that they received too little, and 19% did not remember. Among the non-participants, the corresponding percentages were 36%, 7%, 29%, and 29% (data not shown). Table 3 shows what role the written information sheet played at the time of the consent.

Decision making

Table 4 shows how patients experienced their decision making. In all, 31% of the trial participants and 59% of the non-participants found the decision *difficult* or *relatively difficult* to make (data not shown); 81% of the trial participants would make the same decision again, 1% would not, and 18% did not know. Among the non-participants the corresponding percentages were 48%, 19%, and 33%, respectively (data not shown).

Patients' primary reasons for participating or not participating in the trial are summarised in tables 5 and 6. While 71% of trial participants consented, for reasons that are compatible with an uncoerced and unmanipulated consent (those patients cited a, b, d, e, or j as their primary reason for participating), 29% participated for more dubious reasons (those patients cited c, f, g, h, or i as their primary reason for participating). The patients who cited c, f, g, h, or i as their main reason for participating felt significantly less able to decide at the time of the consent than those who cited a, b, d, e, or j ($\gamma = 0.606$, $p < 0.0005$).

Attitudes to the consent process

In all, 50% of the trial participants gave an affirmative answer to the question ''Do you find it acceptable that patients in your situation have to decide whether or not to participate in a scientific study?''. Twenty six per cent gave a negative answer, and 24% did not know. Among the non-participants, the corresponding percentages were 34%, 51%, and 15% (data not shown). The questionnaires encouraged the patients to comment further. Those patients who found the consent process acceptable gave the following reasons:

- Research is important for the treatment of future patients
- It is important to respect patients' right to decide for themselves
- It is acceptable that patients have to decide in so far as they feel able to decide.

Those patients who did not find the consent process acceptable commented that it was impossible to make a decision under the circumstances; that they did not want to be asked to make any decisions under the circumstances; or that they did not approve of the randomisation. While some

Table 1 Description of the patient population

		n	Age (mean) (years)	Female (%)	Primary angioplasty (%)	Referral hospital (%)
A	Respondents	103	60	25	52	71
	Non-respondents	22	68*	23	50	59
B	Respondents	78	61	30	0	89
	Non-respondents	44	64	34	0	80

*Difference in mean age between respondents and non-respondents was significant (Student's *t* test: p=0.029; 95% confidence interval 0.8 to 13.8).
A, patients who participated in the trial; B, patients who did not participate in the trial.

Table 2 Patients' recollection of information about the trial

		Yes (%)	No (%)	Do not remember (%)
"Did you understand that you were asked whether or not you would participate in a scientific study comparing two treatments?"	A	72	26	2
	B	53	40	8
"Which of the following issues were you informed about?"				
Purpose of the study	A	72	10	17
	B	46	24	31
Potential benefits	A	40	20	39
	B	20	41	39
Potential risks	A	29	32	39
	B	17	49	35
That the treatment I would receive would be decided by drawing lots	A	79	10	11
	B	46	24	30
That participation was voluntary	A	89	3	8
	B	82	4	15
What treatment I would receive if I chose not to participate	A	53	23	25
	B	65	13	23

A, patients who participated in the trial (n = 103); B, patients who did not participate in the trial (n = 78).

patients argued that the doctor should advise the patient in the situation or make the *treatment* decision, only two patients argued that the doctor ought to decide whether or not to enrol the patient in the trial.

DISCUSSION

In this study, most of the trial participants agreed or mostly agreed that they felt capable of deciding whether or not to participate in the trial. Likewise, qualitative interviews with DANAMI-2 participants showed that some patients considered themselves competent at the time of the consent.[11] As it would arguably be morally problematic to exclude from the decision making process any patients with AMI who consider themselves competent, these studies do not support a waiver of informed consent, as has been suggested as an alternative solution.[5 12 13] On the contrary, they indicate that the patient's right to decide whether or not to participate in research should be upheld in such trials. Nonetheless, only half the trial participants found it acceptable that patients in their situation have to decide whether or not to participate in a scientific study. Accordingly, it is pertinent to address the obvious problems of the informed consent process that this study also reveals.

Some 40% of the trial participants felt under pressure at the time of the consent procedure. This pressure, however, is not likely to be caused by medical staff coercing the patients to participate in the trial because, first, the vast majority of patients recall being informed that participation was voluntary, and second, only 2% of the patients participated in the trial because they reckoned that the doctor wanted them to participate. It is more likely that the patients felt pressurised because they were being required to make a decision in an emergency situation despite their medical condition. As many of the patients who did not find the consent process acceptable commented that they did not want to or did not feel able to make a decision, it seems to be of crucial importance not to pressurise patients into decision making if they do not feel able to decide.

Some 22% of the trial participants did not feel able to make the decision at the time of the consent. The fact that the symptoms of AMI can vary considerably may explain why some patients felt fully competent to decide while others clearly did not. In previous studies of the consent process in such trials, there seems to be no consensus as to whether or not patients with AMI are able to decide at the time of the consent. Ågard and colleagues[8] and Smith[5] questioned patients' abilities, while Smithline and colleagues[14] were more optimistic. The latter found that at least 68% of patients were able to give informed consent. Those findings are supported by our survey, in which 76% of the participants agreed or mostly agreed that they felt able to make the decision. The investigators of the recent HERO-2 consent substudy concluded that most of the patients (52%) only met a very basic autonomy criterion—that is, being able to do something rather than nothing.[9] The divergent results in the various studies in relation to patients' competence may reflect an underlying disagreement over the type of cognitive skills that patients must demonstrate to give valid consent. In this survey study, we simply focused on patients' self assessed ability to decide.

A quarter of the trial participants lacked a basic understanding of the decision they had to make as they did not understand that they had to decide whether or not to participate in a scientific study comparing two treatments. Also, other studies of trials in AMI have found that comprehension of the information is incomplete or lacking in a sizeable proportion of the patients.[3–9] In this study only a minority of the trial participants read the information sheet *before* they made the decision and some never read it. The vast majority of non-participants did not read it at all. Other studies confirm that the oral information is the most important source of information in AMI trials.[6–9]

Table 3 The written information sheet

	"When did you read the written information sheet?"				
	Before I made the decision (%)	After I made the decision (%)	I have not read it (%)	Do not remember (%)	Total (%)
A	28	43	25	4	100
B	7	3	80	10	100

A, patients who participated in the trial (n = 103); B, patients who did not participate in the trial (n = 78).

Table 4 Patients' perception of the consent process

			Agree (%)	Mostly agree (%)	Mostly disagree (%)	Disagree (%)	Do not know (%)	Total (%)
''Do you agree with the following statements?''	I felt capable of deciding whether or not to participate in the trial	A	50	26	11	11	3	100
		B	48	15	9	17	12	100
	I felt under pressure when I had to make the decision	A	18	22	10	45	5	100
		B	19	16	10	38	16	100
	I felt that the decision was fully mine	A	70	13	4	9	4	100
		B	72	13	2	3	10	100

A, patients who participated in the trial (n = 103); B, patients who did not participate in the trial (n = 78).

The non-participants in this study were a heterogeneous group comprising patients who did not wish to participate in the trial as well as those who were not informed about the trial because their physician felt that their physical and mental condition was incompatible with an informed consent process. Unfortunately, it was not possible to discriminate between those patients in this survey, and the fact that patients who were not informed about the trial nevertheless received a questionnaire may explain the lower response rate and the relatively poorer recollection of the information among the non-participants. Moreover, some non-participants may have forgotten all about the informed consent process, as they (unlike the trial participants) were not informed repeatedly about the trial after their recovery. Indeed, some non-participants (four patients) phoned to inform us that they had not heard about any trial despite their case records stating that they had been informed about it. The fact that non-participants were not necessarily extensively informed is not morally problematical if those patients did not want to participate in the informed consent process. However, nearly a third of the non-participants found that they received too little information. This indicates that those non-participants who do not explicitly waive the information, and who are able to participate in the consent process, would benefit from an improved information procedure. Very few of the non-participants stated that they did not wish to participate in research. In other words, this study does not indicate that non-participants are sceptical about the research enterprise as such.

Table 5 Patients' main reasons for participating in the trial (n = 103)

		Per cent of respondents
a	I wished to be examined and treated by cardiac experts	26
b	I wanted to help future patients in the same situation	23
c	I wished to be treated as soon as possible and I assumed that it would delay the therapy if I did not consent	15
d	I preferred the treatment that was only available within the trial	12
e	I did not have any misgivings about participating in the trial	8
f	I believed that the doctor thought it would be best for me to participate in the trial	7
g	I was not sure that I would receive the best possible care if I did not consent	3
h	I was not sure what would happen with me if I did not consent	2
I	I believed that the doctor wanted me to participate in the trial	2
j	I wanted to help the progress of medicine	2
	Total	**100**

Strength and weaknesses

The response rates of the survey were favourable, especially for the trial participants who apparently believed the questionnaire survey part of the DANAMI-2 follow up procedures. It is a potential bias, however, that those trial participants who did not return the questionnaire were on average eight years older than the respondents. Conversely, it is not likely that the conclusions would have been notably different had the patients in the study been older, as none of the results was dependent on age. The time lapse of three weeks from the informed consent process to the sending of the questionnaires was intended to be long enough to give patents time to recover and reflect on their experiences in hospital, while at the same time being short enough to ensure that patients were still able to remember the consent process. In-depth interviews with patients three to four weeks after the consent process showed that they were indeed able to remember their experience of the process.[11]

Suggestions for future trials

On the basis of this study, it seems ethically sound to seek informed consent from patients with AMI despite the emergency situation and the medical condition of the patients. It is extremely important that such patients are provided with information which is as concise and simple as possible, although sufficient for them to make an informed decision. As most patients did not read the information sheet before deciding whether to participate in the trial, physicians and research ethics committees (RECs) should focus mainly on improving the oral information. Accordingly, an outline of the oral information should be reviewed by the REC, and the physicians involved in the trial should be briefed about the form and content of this approved outline.

The issue of whether or not patients feel able to decide should be addressed explicitly in connection with the consent

Table 6 Patients' main reasons for not participating in the trial (n = 78)

		Per cent of respondents
a	I was apprehensive about participating	37
b	I wished to be treated as soon as possible and I assumed that it would delay the therapy if I participated	31
c	I did not want lots to be drawn to decide which treatment I would have	18
d	I did not have enough information about the study	7
e	I preferred the treatment I would receive if I did not participate	3
f	I did not wish to participate in research	3
g	Do not know	2
h	I believed that the doctor thought it would be best for me not to participate in the trial	0
	Total	**100**

process. Where they do not feel able to decide, the physician needs to inquire whether they need more information or may prefer not to participate in an informed consent process under the circumstances. Patients who would prefer not to be involved in the process should be excluded from the trial.

Moreover, measures other than the procedures of informed consent are necessary to protect patients against research related harm. First, protocols involving patients with AMI should be reviewed extremely carefully by the responsible REC; and second, an independent data and safety monitoring board, like the safety and ethics committee of the DANAMI-2 trial, should be appointed to evaluate the accumulating data and to ensure that it remains safe to join the trial. Ideally, these measures would take some of the weight of the informed consent process and allow physicians to focus on the basic function of the process—that is, to respect the patient's right to say yes or no. This is the basic function of informed consent which should be upheld in AMI trials despite the difficulties inherent in the process.

Conclusions

Informed consent should be sought in AMI trials despite the emergency situation and the medical condition of the patients. Patients' self assessed ability to make a decision should be explicitly addressed during the consent process, and patients should not be pressurised into decision making. As most patients in our study did not read the information sheet before deciding whether to participate in the trial, physicians and research ethics committees should focus mainly on improving the oral information.

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