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INTRODUCTION

At advanced age, individuals are increasingly prone to develop diseases and multimorbidity is more frequently present. [1] Since life expectancy in developed countries is increasing, [2] research into causes and prevention of disease in the elderly is necessary. Nevertheless, older people are underrepresented in research studies; Bugeja et al reported that one third of research articles in the BMJ, Gut, the Lancet, and Thorax published between June 1996 and June 1997, excluded older adults without justification. [3] McMurdо et al repeated this analysis in 2005, and found that nearly 15% of articles still excluded older adults and that fewer than 5% of published articles focused specifically on older adults. [4] Several explanations for the scarcity of studies among older people may be postulated. [5-7] First, researchers may anticipate barriers to participation such as mobility problems to reach their study centre. Second, impairments (e.g., visual and cognitive) of older people may make it difficult to participate. [8-10] Third, co-morbidities and competing risks among older people may play a role in influencing study outcomes. Because of the lack of inclusion of older persons in key trials, external validation of findings from studies of younger persons to an older population may be questioned. [4,11,12] Furthermore, research studies that are conducted among older people often include the most vital individuals, i.e., without co-morbidities, recent surgery, or hospitalisation, which can make the generalizability of the study results questionable. Therefore, there is a need for research studies among the older people.

The incidence of venous thrombosis increases steeply with age and ~60% of all venous thrombosis events occur in those aged 70 years and older. [13] However, vast majority of studies into etiology, treatment and prevention of venous thrombosis are restricted to younger people. [14] Here we report on factors that affecting the participation of older patients in a population-based case-control studies on the etiology of venous thrombosis among older people (70-80 years). We compared the participation in older patients in the Multiple Environmental and Genetic risk factors for venous thrombosis (MEGA) and the Age and Thrombosis, Acquired and Genetic risk factors in the Elderly (AT-AGE) study. [15]

METHODS

The designs of the MEGA and the AT-AGE study have been described in detail previously. [15,16]. Both studies are population-based case-control studies designed to investigate acquired and genetic risk factors for venous thrombosis. From March 1999 onwards, In the MEGA study, all consecutive patients aged 18-80 years old with a first episode of venous thrombosis (deep venous thrombosis of the leg (DVT), the arm, or a pulmonary
embolism (PE)) were identified via the anticoagulation clinics in the Netherlands (6 clinics: Amersfoort, Amsterdam, Den Haag, Leiden, Rotterdam, Utrecht). From March 2001 until the end of the study in 2004, patients in age 70-80 years were no longer invited due to low agreement rates to participate. In the AT-AGE study, consecutive patients aged 70 and older with a first DVT of the leg or PE between 2008 and 2011, were identified via the anticoagulation clinics in Leiden and Haarlem, the Netherlands and the Vascular Laboratory and the Radiology department of the University of Vermont Medical Centre, Burlington, Vermont, USA. In both the MEGA study and the AT-AGE study, patients with severe psychiatric problems or an inability to speak Dutch or English were excluded. In the AT-AGE study, patients with an active malignancy were also excluded.

For this manuscript we analysed the patients age 70-80 years included in the MEGA study and the AT-AGE study in the Netherlands. Patients were invited in a similar way in both studies, i.e., by means of a personalised invitation letter sent by the anticoagulation clinic followed by telephone contact by a dedicated data manager or trial nurse from the study centre. To allow comparisons in the MEGA and the AT-AGE study, MEGA study participants with active malignancy were excluded from this analysis.

Subsequent data collection differed for the two studies. In the MEGA study a detailed questionnaire on acquired risk factors for venous thrombosis was sent by mail to all patients. Patients who were unable or did not want to fill in the mailed questionnaire were approached by telephone and a short questionnaire was completed during the telephone interview. Blood samples were obtained approximately three months after discontinuation of anticoagulation treatment. If treatment duration was longer than one year, blood was sampled during treatment. For this blood draw all patients were invited to come to the anticoagulation clinic in their region. In the AT-AGE study all participants were visited at home twice. During the first home visit an interview was conducted by a trained research assistant and a detailed questionnaire on acquired risk factors for venous thrombosis was completed. During this home visit, a blood sample was drawn (to obtain DNA and non-vitamin K dependent coagulation factors). One year after the venous thrombosis (when most patients had discontinued anticoagulation therapy), a second home visit was conducted and, another blood sample obtained.

**Analyses**

For this study we calculated the participation rate for filling in a questionnaire (questionnaire participation rate) and for both filling in a questionnaire and donating a blood sample (overall participation rate). In the MEGA study the questionnaire participation rate was determined as the percentage of patients for whom there was a returned mailed questionnaire or for whom a short telephone administered questionnaire was completed. In the AT-AGE study, this was the percentage of patients for whom a first home visit was conducted, during which the study interview was completed. The overall
participation rate was calculated as the percentage of patients that finished the full research study including filling in the questionnaire, and participating for blood sampling (for the AT-AGE study the second blood sample). To investigate whether the participation rate differed with age, we stratified the analyses by age groups 70-75 and 75-80 years old. We also assessed the characteristics of the participating patients in the two studies, such as sex, BMI, and the presence of recent surgery.

**RESULTS**

The participation rate in the two studies is shown in figure 1. In the MEGA study, 446 patients and in the AT-AGE study, 309 patients aged 70-80 years old were eligible to participate. In the MEGA study, 251 patients provided information on the questionnaire (56%) as compared with 224 patients in AT-AGE (72%). In the MEGA study the median time between the venous thrombotic event and the blood draw was 10 months (range 3-25 months) and in the AT-AGE study this was 12 months (range 11-16 months). Of the patients 22 (8.8%) patients died in the MEGA study before the blood draw was performed compared with 11 patients (4.9%) in the AT-AGE study. In the MEGA study, a blood sample was provided by 53% of the patients (122 of 229 patients). In the AT-AGE study this was 89% of the patients (189 of 213 patients). The overall participation (questionnaire participation plus blood draw) was 27% (122/446) in the MEGA study and 61% in the AT-AGE study (189/309) (figure 1). Age-stratification demonstrated that the questionnaire participation rate was similar across the 5-year age-groups within the studies. (MEGA study 70-75 years: 56% (125/223) of which 51% men, 76-80 years: 57% (126/223) of which 52% men. In the AT-AGE study: 70-75 years: 74% (131/178), 76-80 years: 71% (93/131). In the AT-AGE study 48% were men in the 70-75 years old group, and 40% in the 75-80 years old group.

**Table 1. Characteristics of patients of the MEGA and the AT-AGE study**

<table>
<thead>
<tr>
<th></th>
<th>MEGA study (70-80 years) N(%)</th>
<th>AT-AGE study (70-80 years) N (%)</th>
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<tbody>
<tr>
<td>Questionnaire participation</td>
<td>251</td>
<td>224</td>
</tr>
<tr>
<td>Men, N (%)</td>
<td>130 (51.8)</td>
<td>100 (45.0)</td>
</tr>
<tr>
<td>DVT without PE, N (%)</td>
<td>148 (59.0)</td>
<td>87 (38.8)</td>
</tr>
<tr>
<td>Median BMI kg.m-2 (range)</td>
<td>25.9 (17.1-53.0)</td>
<td>26.8 (18.0-43.3)</td>
</tr>
<tr>
<td>Hospitalisation(%)</td>
<td>23 (9.2)</td>
<td>72 (32.1)</td>
</tr>
<tr>
<td>Surgery(%)</td>
<td>20 (8.0)</td>
<td>50 (22.3)</td>
</tr>
</tbody>
</table>

N = number, DVT= deep venous thrombosis, BMI = Body Mass Index
MEGA: Multiple Environmental and Genetic risk factors for venous thrombosis
AT-AGE: Age and Thrombosis, Acquired and Genetic risk factors in the Elderly
Characteristics of the participating patients in both studies are shown in Table 1. Patients included in the MEGA study were diagnosed more frequently with DVT only (59%) than patients in the AT-AGE study (39%). Hospitalisation and surgery three months prior to the thrombosis were more frequently present in the AT-AGE study than the MEGA study.

<table>
<thead>
<tr>
<th></th>
<th>MEGA study</th>
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<tbody>
<tr>
<td>Total eligible Patients</td>
<td>446</td>
</tr>
<tr>
<td>Questionnaire Participation</td>
<td>251 (56%)</td>
</tr>
<tr>
<td>Overall Participation</td>
<td>122/446 (27%)</td>
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</tbody>
</table>

**Figure 1.** Participation rates in the MEGA and the AT-AGE study

**DISCUSSION**

In this study we show that participation rate of older patients in research is substantially increased (from 27% up to 61%) when home visits were used. Questionnaire participation via a structured interview during a home visit is superior to asking participants to complete a mailed questionnaire (72% versus 56% completion). Participation did not differ among those aged 70-75 compared to 75-80.

Reasons for higher participation via an in-home visit in old patients with thrombosis are likely related to mobility and social aspects, i.e., already having frequent hospital trips, reluctance to ask assistance of caregivers to participate in research, and a lack of personal contact with investigators for a mailed questionnaire. Visual or cognitive impairment are also more likely to deter participation in a questionnaire as compared to a home visit as participants may gain confidence when a research co-worker is assisting them to answer the questions. Davies et al. previously reported on the role of the distance between study site and the person’s residence and the importance of
minimising the participant reluctance to participate in the New Castle 85+ study. [9] Moreover, it was previously recognised that the personal contact of a researcher during a home visit encourages older adults to be more dedicated to the research study, and thus to participate for a longer period. [17] Comparing the percentages of older patients with hospitalisation and surgery, we found higher prevalences in AT-AGE than in the MEGA study. This indicates that home visits increased participation rates also in the most vulnerable group. Unfortunately, we do not have reliable data on characteristics of the non-responders and the reasons why patients were not able or willing to participate. We cannot rule out that other study differences apart from the ones described here may explain a difference in the participation rate, e.g., in the AT-AGE study it was emphasised to the patients that this study was specifically focused on the older adults and this might have increased willingness to participate.

In conclusion, as the MEGA and the AT-AGE study were both performed in the same region (the Netherlands), study the same disease (venous thrombosis), and were performed by the same investigators, we had the opportunity to compare the participation rates among older patients when using different approaches for inclusion. Home visits were an effective approach to increase the participation rate in this age group.
REFERENCES


