Comorbidity and treatment decision-making in elderly non-Hodgkin’s lymphoma patients: a survey among haematologists

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ABSTRACT

Background: Elderly patients with non-Hodgkin’s lymphoma (NHL) are often not treated with standard immunochemotherapy and this might have a negative impact on their survival. Little is known about the determinants that play a role in treatment decision-making of clinicians regarding elderly patients with NHL. The objective of this study was to gain more insight into these determinants.

Methods: A survey was conducted amongst haematologists in the Netherlands. The survey contained questions about comorbidity, polypharmacy, social setting, nutritional status, depression, mild cognitive impairment, dementia, activities of daily living (ADL) and instrumental activities of daily living (IADL) in relation to treatment decisions in elderly NHL patients.

Results: Of all comorbidities, respondents designated cognitive disorders and cardiovascular comorbidity as the most important factors when assessing whether an older patient with NHL is eligible for curative treatment. Also in decreasing degree of importance ADL, IADL and depressive disorder are frequently included in treatment decision-making. Almost half of the respondents feel that treatment of the elderly person is complicated as a result of a lack of scientific evidence.

Conclusion: Haematologists are aware of coexisting problems in elderly patients and they frequently take comorbidities, cognitive disorders and functional status into consideration in treatment decision-making. Future studies are needed to determine the exact role that these factors should play in the treatment of elderly patients. Furthermore, haematologists feel that treatment of the elderly is complicated and there is a lack of scientific evidence, and therefore older adults should be better represented in clinical trials.

KEYWORDS

Comorbidity, elderly, non-Hodgkin’s lymphoma, survey.

INTRODUCTION

In 2007, 1572 patients were diagnosed with aggressive non-Hodgkin’s lymphoma (NHL) in the Netherlands and it is expected that the incidence will increase to almost 1900 patients in the year 2020 due to ageing of the population and increasing incidence with advancing age.1 Currently, the median age at diagnosis is 66 years.4 Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of aggressive NHL. The first choice of treatment for DLBCL is the rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) regimen. This improves complete remission rates and survival, in young as well as in elderly patients.1,4 However, treatment of elderly patients with aggressive NHL can be complicated because of additional factors such as comorbidity and polypharmacy. Furthermore, elderly patients are often under-represented in clinical trials and only relatively fit elderly patients are included. Therefore...
most evidence is based on a selection of patients.\textsuperscript{13-14} There are only a limited number of population-based studies with unselected elderly DLCBL patients. These also show that R-CHOP is associated with improved survival in comparison with other treatment strategies.\textsuperscript{9,14-15} Nevertheless, elderly NHL patients are often not being treated with standard immunochemotherapy.\textsuperscript{5-8,10,15} Motives for suboptimal treatment are amongst others poor performance status and comorbidity, but also high age in itself is declared by physicians to be a reason for refraining from optimal treatment.\textsuperscript{5-8,15}

Little is known about the determinants that might play a role in the decision-making of clinicians regarding the eligibility of elderly patients with a haematological malignancy to be treated with curative intent. Therefore, we conducted a survey among haematologists in the Netherlands to gain insight into these determinants. The emphasis was on DLBCL, as this type of aggressive NHL can be treated with curative intent.

**METHODS**

**Data collection**

Haematologists were invited to complete the online questionnaire ‘Treatment of the elderly with a haematological malignancy’ on behalf of the Dutch-Belgian Cooperative Trial Group for Haemato-Oncology (HOVON). HOVON is a foundation that focuses on improving and promoting treatment methods for adult patients with malignant haematological disorders.\textsuperscript{16} Haematologists were invited to participate through e-mail in November 2011. Non-respondents were sent a reminder e-mail within two months.

**Study measures**

The questionnaire contained questions about the importance of various factors that might play a role in the decision-making of clinicians regarding treatment with curative intent in elderly patients. There were nine questions regarding the extent to which respondents agree that various comorbidities, polypharmacy, social setting and nutritional status should be taken into consideration. In addition, there were five items regarding the frequency with which depression, mild cognitive impairment, dementia, activities of daily living (ADL) and instrumental activities of daily living (IADL) are taken into account. The application of chemotherapy dose reductions in advance and refraining from curative treatment in relation to toxicity was assessed. Furthermore, the respondents were asked to what extent they feel that treatment of older adults with haematological malignancies is complicated because of a lack of scientific research and to what extent respondents exclusively treat elderly patients if they can be included in clinical trials.

Also the respondents’ age and gender were assessed, as well as the type of hospital they work in. In the Netherlands, three types of hospitals can be discerned: university hospitals, tertiary medical teaching hospitals (STZ) and general hospitals. STZ hospitals are large teaching hospitals, where highly specialised care is provided.\textsuperscript{17}

**RESULTS**

Invitations to complete the questionnaire were sent to 255 haematologists. A total of 94 questionnaires were returned (36.5\% response rate), of which 87 were fully completed and seven were incomplete (table 1). The mean age of the respondents at the time of survey was 49.6 years. There were more male than female respondents. Of the respondents, 29.8\% worked at a university hospital, 33.0\% at an STZ hospital and 37.2\% at a general hospital.

The two comorbidities that respondents designated as most important when assessing if an elderly patient qualifies for a curative treatment intent (answer categories totally agree and agree combined) were cognitive disorders (99\%) and cardiovascular comorbidity (95.7\%) (figure 1). These were followed by pulmonary comorbidity (88.3\%), nutritional status (84.1\%), social setting (79.8\%), kidney disease (70.2\%), mobility disorders (61.7\%), liver disease (57.4\%) and polypharmacy (57.4\%).

Respondents frequently include dementia (89\%, answer categories always and often combined) and ADL (85.7\%) in treatment decision-making in elderly patients with a haematological malignancy. IADL (69.4\%), depressive disorder (53.2\%) and mild cognitive impairment (41.3\%) are less often taken into account (figure 2).

Twenty-three percent of the respondents often apply dose reductions in elderly patients to avoid estimated toxicity, while only 2.3\% of respondents regularly refrain from treatment with curative intent for toxicity reasons (answer category ‘Always’ and ‘Frequently’ combined) (table 2). Of

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being treated with chemotherapy is reduced and the risk of toxicity is increased. And lastly, in various studies a relation was observed between survival and nutritional status, cognition, frailty, IADL, ADL and depression, but this could not be confirmed in other studies. As a result of these inconsistent study results, the interpretation of coexisting diseases in elderly patients with regard to treatment consequences is complicated and more research in this field is necessary.

Interestingly, respondents state that they regularly take comorbidities, cognitive disorders, the patients' social setting, nutritional status, ADL, IADL and depression into consideration when making treatment decisions. However, in daily clinical practice systematic assessments are rarely carried out to identify problems in these areas; this is, among other reasons, because it is time consuming. In general, the physicians' judgment is used to estimate whether there are additional problems, even though it is known that this is not very reliable. Comprehensive assessment results in the detection of a higher number of previously unknown geriatric problems than the physicians' judgment, although it is still not known how to adjust treatment decisions based on comprehensive geriatric assessments.

Finally, a large proportion of the respondents feel that treatment of the elderly is difficult, because relatively little scientific research has been done among this population. Indeed, older adults are poorly represented in clinical trials, due to direct age-based exclusion as well as due to restrictive inclusion criteria, selecting for the fittest elderly. Since the majority of all DLBCL patients are elderly, it is important that they are better represented in randomised controlled trials so that treatment of this population can be improved.

The current study has some limitations. We did not define the term 'elderly patient', but left this to the interpretation of the respondent. Furthermore, we cannot exclude that haematologists with a special interest for elderly patients with NHL responded. However, there are no direct indications for this. The strengths of our study are that this is, to the best of our knowledge, the first study investigating the determinants that influence treatment decision-making. In addition, it is a multicentre study including haematologists from university hospitals as well as STZ hospitals and general hospitals and the participation rate of the haematologists was high. Therefore we are confident that the results of our study are generalisable.

In conclusion, haematologists are well aware of coexisting problems in elderly patients and comorbidities, cognitive disorders and functional status are frequently included in treatment decisions. There is, however, no convincing evidence of the exact role comorbidity should play in the treatment of elderly NHL patients. Moreover, clinicians feel that treatment is complicated due to a lack of scientific evidence. Therefore, future studies should address this problem and older adults should be better represented in clinical trials, so that evidence-based guidelines for the treatment of elderly patients with a haematological malignancy can be developed.

ACKNOWLEDGEMENTS

We thank all the haematologists for their participation in the study.

DISCLOSURES

Celgene B.V financially supported M.W.M. van der Poel, G.J. Ossenkoppele, E. Maartense, P. Wijermans, M. Hoogendoorn and H.C. Schouten for participation in an advisory board. Celgene B.V had no further role in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

W.J. Mulder has declared no conflict of interests.

REFERENCES


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