Australian clinicians' perceptions of patients with very high risk of fracture

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Abstract

Background: International osteoporosis guidelines have recommended treatment approaches based on fracture risk stratification, in particular anabolic therapy for patients with very high risk (VHR) of fragility fracture. The aim of this study was to summarize Australian clinicians' perceptions of patients at VHR of fracture.

Methods: Australian clinicians invited to educational webinars on anabolic treatments for osteoporosis were surveyed in March and April 2021. The survey included 23 questions on patient characteristics and treatment approaches for a patient that the survey participant had most recently seen and identified to be at VHR of fracture.

Results: Of the 268 clinician attendees who were invited to complete the post-webinar surveys, 67 (25%) responded and permitted publication of aggregated data. A typical patient perceived to have a VHR of fracture was a woman in her 80s, living at home, who had been diagnosed with osteoporosis between 5 and 10 years ago, and received treatment for 1 to 5 years' duration, most commonly denosumab. The patient frequently had a T-score below –3.0 SD (standard deviation), multiple fragility fractures and most commonly suffered a vertebral fracture in the past 12 months, whilst on an adequate regimen of osteoporosis medication. There was a mismatch between the patient being eligible for anabolic therapy (64.2%) and actually having been prescribed an anabolic treatment in the past (20.9%).

Conclusions: This study provided a snapshot of Australian clinicians' perceptions of patients with a VHR of fracture. Local reimbursement criteria heavily influenced perceptions of Australian clinicians on VHR and the use of anabolic agents. The mismatch between patients deemed eligible for reimbursed anabolic therapy and those prescribed an anabolic agent, suggest treatment inertia. Further qualitative exploration of the reasons for the clinicians' perceptions are needed. Differing definitions for VHR need inclusion in local osteoporosis guidelines.

Background

Osteoporosis is a growing global public health concern with fragility fractures significantly impacting patient quality of life and increasing mortality risk.(1, 2) Key international osteoporosis guidelines have recently placed a strong emphasis on risk stratification and characterized groups of patients with osteoporosis with a very high risk (VHR) of future fractures.(2–4) The guidelines advocate risk stratification as a way to tailor the therapeutic approach.(2, 4) For those at very high risk of fracture, early intervention using agents with a rapid effect on reducing fracture risk, such as anabolic drugs, is warranted.(2–4) Stratification also allows long-term treatment strategies to be considered, including sequencing, at the time of initial therapy selection.(2–4)

Anabolic treatment options have broadened and now include romosozumab, an anti-sclerostin monoclonal antibody.(3) Romosozumab has demonstrated potent fracture efficacy and gains in bone mineral density in controlled clinical trials.(5, 6) Romosozumab has been approved for use in Australia

since July 2019 and from April 2021, was approved for reimbursement for patients with severe established osteoporosis at VHR of fracture as defined by a BMD (bone mineral density) T-score of ≤−3.0 SD and multiple fragility fractures, with at least one symptomatic fracture within the previous 12 months whilst on adequate doses of an antiresorptive agent.(7) However, current Australian osteoporosis guidelines do not have a definition for patients at VHR of fracture. Moreover, anabolic treatment is only considered as second-line therapy as per the criteria for reimbursement.(7)

There are currently no data on how Australian clinicians practically define VHR of fracture in osteoporosis patients and thus the aim of this study was to collate and summarize Australian clinicians' perceptions of patients at VHR of fracture.

Methods

Study design

The study design consisted of a post-webinar survey of Australian clinicians who attended at least one of two Amgen-sponsored webinars on anabolic treatments for osteoporosis, which were held in March and April 2021. For the first webinar, approximately 60 clinicians who had experience with prescribing anabolic therapy were invited. For the second webinar, over 500 clinicians who were interested in learning more about anabolic therapies, specifically romosozumab, were invited. Across the two webinars, 268 clinicians attended. The webinar content included data presentation from key clinical trials of anabolic therapies, the types of patients appropriate for anabolic therapy and clinical scenarios with practical considerations. At the end of each webinar, all attendees were invited to complete the survey. A total of 76 attendees completed the surveys, but only 67 attendees consented to their aggregated data forming part of this publication.

Survey questions

The survey was developed by the webinar sponsor in collaboration with the authors and related to a patient that the survey participant had most recently seen and identified to be at VHR of fragility fracture (see Appendix for full list of questions). Twenty-four questions were posed, relating to the patient's demographic information (sex, decade of birth [between 1920s to 1990s], and living arrangements [at home independent living, assisted living arrangement, or nursing home]), time since diagnosis of osteoporosis (categories from <5 years to >15 years) and the criteria used for diagnosis (T-score ≤−2.5 SD, fragility fracture or both), and current BMD (T-score: >−1.0, −1.0 to −2.5, −2.5 to −3.0 and ≤−3.0 SD) and past BMD (ever having had a BMD T-score ≤−3.0 SD) measurements. Questions relating to the patient's fracture history included the number of prior fractures (0 to >3), time since last symptomatic fracture (categories from <1 year to > 5 years), anatomic location of last symptomatic fracture and whether the patient had experienced the fracture whilst being treated with antiresorptive therapy for more than one year.Questions relating to the patient's treatment included their current osteoporosis medication (denosumab, oral or intravenous bisphosphonate, or other), duration of treatment (categories from <1

year to > 10 years), their eligibility for anabolic treatment and whether the patient had been prescribed an anabolic agent previously. Participants were also asked to rate their willingness and comfort with initiating anabolic treatments in patients who meet the reimbursement criteria for anabolic treatments.

Ethics approval and informed consent

As per the Australian national guidelines on ethics requirements (The National Statement on Ethical Conduct in Human Research (2007))(8), ethical approval was deemed unnecessary as this study did not investigate individual patient data, but only investigated clinicians' perceptions. Clinicians were made aware that responses would be analyzed as part of a research undertaking and were able to opt out if they declined to participate.

Consent for Publication

Not applicable

Statistical analysis

This was a descriptive study, and statistical analyses were not planned before the survey was taken. The data are presented as numbers and percentages of respondents, or a combination thereof. Categorical data (e.g. age, time since osteoporosis diagnosis, duration of osteoporosis treatment etc.) are presented as medians. All analyses were conducted using Microsoft Excel.

Results

Participating clinicians

Overall, of the 268 clinician attendees who were invited to complete the post-webinar surveys, 67 (25%) responded and permitted publication of aggregated data. Out of the 67 responders, the area of specialty was identified for 50 respondents. The majority of respondents were endocrinologists (34/50, 68%), followed by geriatricians (7/50, 14%), rheumatologists (4/50, 8%), internal medicine specialists (3/50, 6%) and general practitioners (2/50, 4%). Out of the 67 responders, 18 respondents were specifically invited to the first webinar as they had experience with prescribing anabolic therapies. Those invited to the second webinar were those who were interested in learning more about anabolic therapy, particularly romosozumab.

Perceptions of patients with very high fracture risk

Based on the medians or modal responses in the survey (see Table 1), a typical patient perceived to have a VHR of fracture was a woman in her 80s, living at home, who had been diagnosed with osteoporosis between 5 and 10 years ago, and received treatment for 1 to 5 years' duration, most commonly

denosumab. Over half (53.7%) of patients had a current T-score below –3.0 SD and 34.3% had a current T-score between –2.5 and –3.0 SD, but 76% had recorded a T-score below –3.0 SD at some point. Most (88%) of the patients had two or more fragility fractures. Patients most commonly (49.3%) suffered a symptomatic vertebral fracture in the past 12 months, whilst on an adequate regimen of osteoporosis medication.

[Insert Table 1 here]

Treatment inertia in initiating anabolic therapy

Treatment patterns described for the sample patients that participants considered to be at VHR of fracture suggested clinician inertia in initiating anabolic therapy. There was a mismatch between the patient being eligible for anabolic therapy (64.2%) and actually having been prescribed an anabolic treatment in the past (20.9%); Figure 1A). The proportion of patients considered eligible for anabolic therapy was three-fold higher than the proportion of patients who had previously been prescribed an anabolic therapy. This represents a treatment gap and opens up a question of inertia for anabolic prescription even amongst experts.

At the end of the educational meetings, the proportion of clinicians who were “very confident” or “confident” about prescribing anabolic therapy was similar to the proportion of positive responses regarding their willingness to prescribe anabolic therapy (Figure 1B and 1C).

[Insert Figure 1 here]

Figure 1: (**A**) Proportion of patients considered eligible for anabolic therapy and previously prescribed anabolic therapy; (**B**) clinicians’ confidence with prescribing anabolic therapy; (**C**) clinicians’ willingness to prescribe anabolic therapy to the VHR patient in question.

Discussion

To our knowledge, this is the first study to capture clinicians’ perceptions of patients with VHR of fracture. Identifying these patients early is important as there is a limited window of opportunity for patient acceptance of more intensive interventions following a fracture.(9, 10) This study helps identify the knowledge gaps around clinicians’ understanding of very high fracture risk and informs the direction of future efforts toward Australian guideline development and education to improve the rates of identification and treatment of patients at VHR of fracture.

The profile of a typical patient that Australian clinicians perceived as being at VHR of fracture showed areas of alignment, as well as some deviations from the characteristics described in international guidelines. For example, although age is a strong risk factor for fracture, the proportion of patients with VHR in a given age bracket does not appear to change dramatically based on UK simulations.(4) Our survey suggests Australian clinicians associate VHR with much older female patients; however, the UK

modelling showed the proportion of VHR patients in those aged ≥50 years, is relatively unchanged. (4) The perception that the VHR category applies only to the very elderly may mean clinicians miss younger VHR groups such as those taking medications causing bone loss.

The recency, number and site of fractures were important factors in the Australian clinicians' perceptions of VHR patients being aligned with international guidelines.(2, 4) In our study, 94% of respondents stated that the VHR patient had a fracture within five years and 54% within the previous year; 88% of respondents stated that the VHR patient had more than two fractures and for 49% of respondents, the recent fracture of concern was a vertebral fracture. These findings are supported by previous studies on recurrent fractures, which showed the risk of recurrent fracture is highest in the first one to five years(9, 11, 12) and that vertebral fractures were associated with the highest absolute risk of a subsequent clinical fracture within 12 months.(11)

Australian clinicians' perceptions of VHR patients strongly aligned with reimbursement criteria for anabolic therapies. This survey was taken at the end of an educational event that emphasized the Australian reimbursement criteria for anabolic therapies, and it may suggest an influence of the reimbursement criteria on clinicians' understanding of VHR. Despite the body of evidence that supports the use of anabolic treatment as first-line therapy in VHR patients(5, 6, 13), given the restrictions of the reimbursement criteria and the high cost of anabolic therapy for privately-funded prescriptions, the clinicians' recall patient may also have been biased toward the reimbursement criteria by their clinical experience. This was even found after an instructive webinar discussing the specific patient groups to benefit from anabolic therapies, distinct from reimbursement criteria. Some clinicians perceived indications that departed from the reimbursement criteria, which reinforces that the recall patient was different for each clinician. Nonetheless, the restrictions of the reimbursement criteria are a major barrier for prescribing anabolic therapies in the sequence that is supported by key clinical studies, thus it heavily impacts the working definition of VHR in the Australian context.(5, 13, 14) More detailed qualitative studies are needed to understand the reasoning behind Australian clinicians' perceptions on the working definition of VHR.

Our results indicate a significant mismatch between numbers of patients eligible for, and those prescribed, an anabolic therapy – the former being three-fold higher than the latter. This suggests inertia in clinicians' prescribing an anabolic therapy. Treatment inertia has been frequently reported in other chronic conditions when patients need to be given daily injectable therapies (e.g. insulin for patients with type 2 diabetes) after they have failed less onerous first-line treatment.(15) Prior to the time of our survey, teriparatide was the only available anabolic agent and prescription rates of this agent was low according to the Australian Medicare claims database.(16) There may have been other patient factors that led to low rates of anabolic therapy prescription, for example, low acceptance of teriparatide or daily injections, or cost of therapy.

The main strength of this study is that it captures perceptions of VHR patients who are 'top of mind' among clinicians in a real-world setting. The study also compared perceptions of VHR patients among

Australian clinicians with local reimbursement criteria for anabolic therapies and VHR characteristics defined in key international guidelines. The main limitations of this study are the small sample size and selection bias, as the survey respondents were mainly a group of specialist clinicians with an interest in anabolic therapies, many of whom had previously prescribed anabolic therapy. Another limitation in the study was that only a limited range of contributing factors to VHR was assessed, and other potent drivers of fractures such as the effect of polypharmacy, comorbidities and non-clinical factors such as falls risk, were not addressed. While this study did not address the full spectrum of risk factors, it is nonetheless an important first step toward thinking about which factors are important for Australian clinicians to consider in stratifying patients according to risk level. Finally, there were only 16.4% of clinicians who recalled a male patient while the rest recalled female patients, despite reimbursement for anabolic drugs being applicable to both sexes. These data could be seen as having limited generalizability of responses. However, the patient recall related to the clinicians' recent experiences and perceptions, providing a snapshot of clinicians' ideas on anabolic treatment indications.

Conclusions

In conclusion, this study provided a snapshot of Australian clinicians' perceptions of patients with a VHR of fracture. The profile of a typical patient that Australian clinicians perceived as VHR was most commonly an elderly woman with multiple fractures, often a recent vertebral fracture, and very low BMD. These features closely aligned with local reimbursement criteria. Further qualitative exploration of the reasons for the clinicians' perceptions are needed; however, this study is an important first step toward thinking about which factors are important for Australian clinicians in their consideration of candidates for anabolic therapy. Development of local guidelines to further characterize groups of VHR fracture patients may enable clinicians to be more confident, overcome inertia and be proactive in prescribing anabolic therapy.

Abbreviations

BMD
bone mineral density
SD
standard deviation
VHR
very high risk

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Of the 76 attendees who completed the surveys, 67 consented to their aggregated data forming part of this publication.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Amgen facilitated the collection of data in this publication during an Amgen-sponsored education program. Prof. Ebeling and Assoc Prof. Girgis were provided honoraria to present the education events.

Funding

Dr Yoonah Choi was remunerated as a consultant medical writer to assist in the development of the education content. The authors did not receive payment for writing this publication, which was produced independently from Amgen.

Authors' contributions

CG and PE developed the “Anabolic Patient Identification Questionnaire”, analyzed and interpreted the survey responses, and reviewed and provided input on all drafts of the manuscript. YC also interpreted the survey responses and assisted in writing the manuscript. All authors read and approved the final manuscript.

Acknowledgements

Not applicable

Consent for Publication

Not applicable

Ethics approval and informed consent

As this study did not investigate individual patient data, but only investigated clinicians’ perceptions, ethical approval and patient informed consent were deemed unnecessary.

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Tables

Table 1: Summary of clinicians' responses (N=67) when asked about their most recent patient with very high risk of fracture

Patient variables	Response, n (%)
Sex of patient:	
Female	56 (83.6)
Male	11 (16.4)
Decade when patient was born:	
1920s	1 (1.5)
1930s	12 (17.9)
1940s	27 (40.3)
1950s	18 (26.9)
1960s	7 (10.4)
1970s	2 (3.0)
Living arrangements:	
At home, independent living	56 (83.6)
Assisted living arrangements	9 (13.4)
Nursing home	2 (3.0)
Estimated time since osteoporosis diagnosis:	
Less than 5 years ago	17 (25.4)
Between 5 and 10 years ago	32 (47.8)
Between 10 and 15 years	10 (14.9)
More than 15 years ago	7 (10.4)
no response	1 (1.5)
Reason for osteoporosis diagnosis:	
Fragility fracture	20 (30.0)
T-score ≤ -2.5	5 (7.5)

Patient variables	Response, n (%)
T-score ≤−2.5 and a fragility fracture	42 (62.7)
Patient's current BMD:	
T-score −1.0 to −2.5	8 (11.9)
T-score −2.5 to −3.0	23 (34.3)
T-score lower than −3.0	36 (53.7)
Patient ever having had a BMD ≤−3.0:	
No	15 (22.4)
Yes	51 (76.1)
No response	1 (1.5)
Number of fractures:	
0	1 (1.5)
1	7 (10.4)
2	34 (50.7)
3	11 (16.4)
> 3	14 (20.9)
Time since last symptomatic fracture:	
Less than 1 year ago	36 (53.7)
1 to 5 years ago	27 (40.3)
More than 5 years ago	3 (4.5)
No response	1 (1.5)

Patient variables	Response, n (%)
Location of recent symptomatic fracture:	
Hip	10 (14.9)
Wrist	7 (10.4)
Spine	33 (49.3)
Pelvis	6 (9.0)
Ribs or breast bone (sternum)	3 (4.5)
Shoulder	1 (1.5)
Upper arm (humerus)	3 (4.5)
Other	3 (4.5)
No response	1 (1.5)
Current osteoporosis treatment:	
Denosumab	37 (55.2)
Intravenous bisphosphonate	10 (14.9)
Oral bisphosphonate	6 (9.0)
Other	13 (19.4)
No response	1 (1.5)
Treatment duration:	
Up to 1 year	9 (13.4)
Between 1 to 5 years	40 (59.7)
Between 5 to 10 years	12 (17.9)
Over 10 years	5 (7.5)
No response	1 (1.5)
Any subsequent symptomatic fractures sustained while patient had been treated for ≥1 year with antiresorptive therapy:	
Yes	48 (71.6)

Patient variables	Response, n (%)
No	18 (2.7)
No response	1 (1.5)

Figures

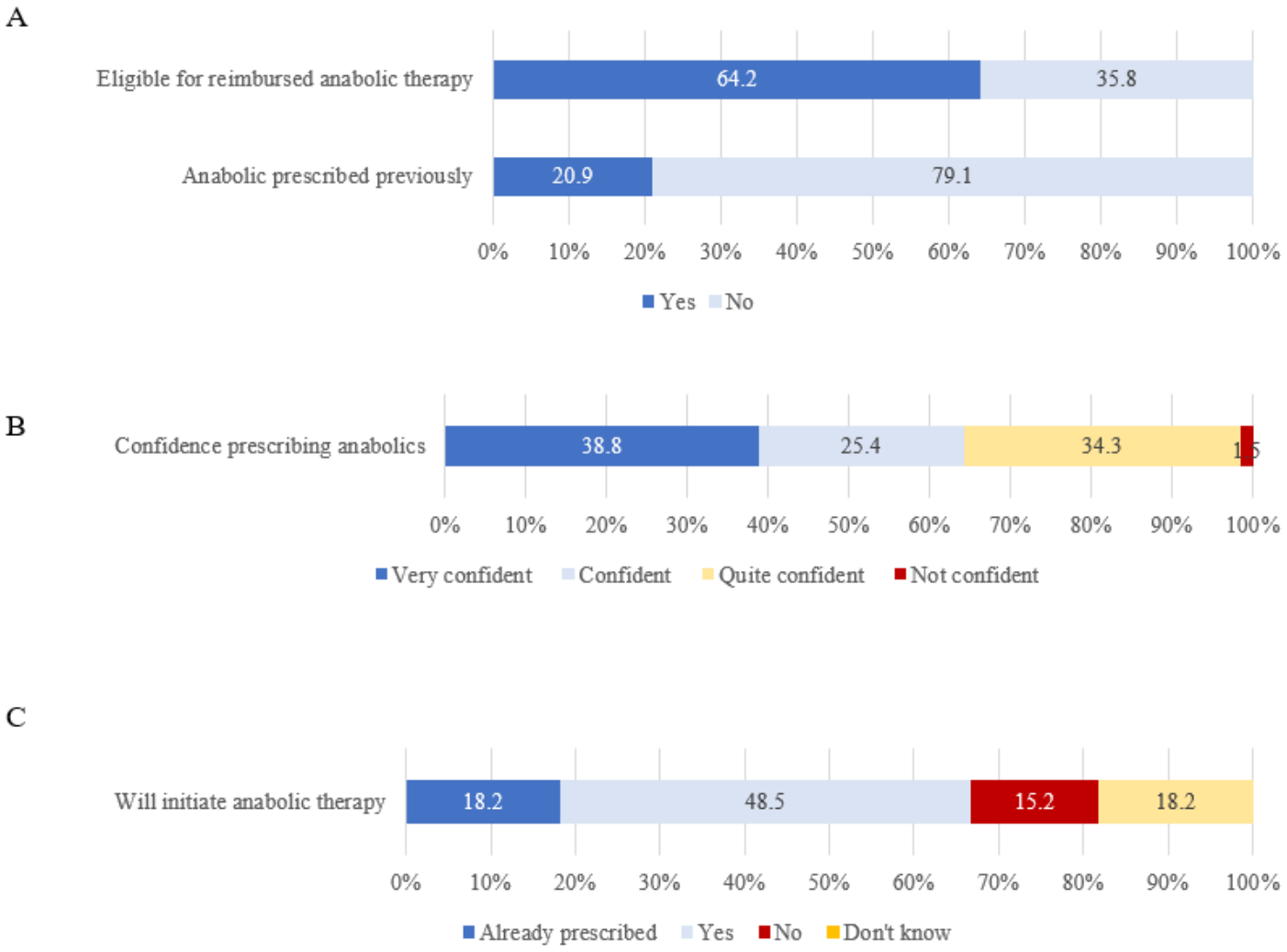

Figure 1

(**A**) Proportion of patients considered eligible for anabolic therapy and previously prescribed anabolic therapy; (**B**) clinicians' confidence with prescribing anabolic therapy; (**C**) clinicians' willingness to prescribe anabolic therapy to the VHR patient in question.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Girgisetal.VHRMSAppendix.docx