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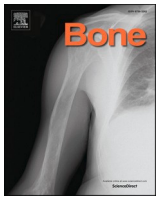

Full Length Article

Characteristics of patients with very high fracture risk in a community-dwelling geriatric cohort

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ABSTRACT

Objective: Bone anabolic treatment has been shown to be superior to oral bisphosphonates, especially in osteoporosis patients with a very high fracture-risk. The current German osteoporosis guideline classifies the very high 3-year fracture-risk based upon a novel fracture-risk model. As age is a severe risk-factor, we examined the distribution and associations to geriatric assessment parameters of the very high-risk group in a well-characterized cohort of community-dwelling geriatric patients.

Methods: Analyses were based on 166 patients (mean age 82 ± 6 years) taken from MUSAR (MUnich SArcopenia Registry). Fracture-risk was calculated as described in the current German guideline. Thereupon, patients were allocated to the low−/moderate (<5 %), high- (5–10 %) or very high-risk group (>10 %). Associations of geriatric assessment parameters with the group allocation to the fracture-risk group were evaluated by covariate-adjusted linear regression analysis.

Results: >80 % of the study population were at an increased fracture-risk. Besides, >50 % were allocated to the very high-risk group. Patients in the very high-risk group showed limitations in all physical performance tests (short physical performance battery (SPPB), gaitspeed, handgrip strength and chair rise test). Also, polypharmacy and a risk for malnutrition (from mini nutritional assessment short form (MNA-SF)), were present. All parameters showed significant associations with group allocation to very high-risk group.

Conclusion: Most of the geriatric patients are at a very high-risk for osteoporotic fractures. Also, this group presented several limitations in the comprehensive geriatric assessment highlighting the vulnerability of this group. Clinicians need to reinforce fracture-risk assessment and familiarize with treatment options.

1. Introduction

In 2023 an updated version of the German S3-guideline on osteoporosis including a new fracture risk calculation model was published [1]. Over the last years many guidelines have included a (very) high-risk group for which bone anabolic treatment is recommended [2–5]. However, there is still no unique definition of the very high-risk group [6]. Most often geriatric patients are considered as being at a very high-risk when the calculator threshold of a fracture risk tool (e.g., FRAX [7]) exceeds a pre-defined limit [3,4]. In some definitions also additional clinical risk factors which are not included in the fracture risk tool are considered [8–10].

The new German risk model addresses this issue and clearly defines four different risk groups (< 3 %, 3–5 %, 5–10 %, > 10 %) for a vertebral or hip fracture within the next three years and also provides treatment recommendations. The evaluation of the fracture risk is based on 33 predefined clinical risk factors, including the Timed-up and Go-Test (TUG), laboratory findings and factors increasing the imminent fracture risk such as history of falls and long-time glucocorticoid intake that have shown profound associations with an increased risk for an osteoporotic fracture of the hip and/or vertebrae in previous studies [1]. Additionally, fracture risk calculation is also possible when no bone mineral density measurement is available [1]. The very high-risk group is defined as the one exceeding the >10 % fracture risk for which bone anabolic treatment is recommended as first-line therapy [1].

As especially geriatric patients are at a severe risk for osteoporosis and are strongly affected by the consequences of fractures we aim (i) to investigate the percentage distribution in the high-risk and very high-risk groups in a community-dwelling geriatric cohort based on the new fracture risk calculator of the German guideline in a retrospective

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analysis.

Additionally, as the TUG as a marker of physical performance was integrated in the latest guideline as one of the risk factors for fracture risk calculation, we aim (ii) to investigate the associations of further variables from a comprehensive geriatric assessment on the fracture risk.

2. Material and methods

2.1. Patients

Data were taken from MUnich SArcopenia Registry (MUSAR). Since July 2018, the registry includes data from patients with a positive SARC-F (strength, assistance with walking, rising from a chair, climbing stairs, and falls) screening, probable or confirmed sarcopenia attending the geriatric day care-hospital at the Ludwig-Maximilians-University hospital in Munich, Germany. Inclusion criteria are: age $\geq$ 65 years, positive SARC-F screening, hospital stay at acute geriatric ward or geriatric day care clinic at LMU Munich Hospital and being able to give consent to the participation. Exclusion criteria are: age $<$ 65 years and not being able to give informed consent.

During every contact with the study center, we conducted a clinical, sociodemographic and psychiatric anamnesis and assessed physical performance and Activities of Daily Living (ADLs), as well as the osteoporosis-status. In this cross-sectional analysis data from baseline evaluation from all available patients between July 2018 and December 2023 (n = 166) were included.

2.2. Risk factor evaluation and fracture risk group allocation

The required variables were either taken from our database (MUSAR) or from the doctor's report. The fracture risk was calculated based on the 33 pre-defined risk factors that were defined in the fracture risk model of the latest S3-guidelin on osteoporosis (supplement Table 1) [1]. For risk calculation the two highest risk factors from different risk groups were multiplied. The fracture risk group was identified by comparing the calculated fracture risk to the provided threshold tables (supplement Table 2). As in daily clinical practice no therapeutic differences between the <3 % and the 3–5 % groups are made, the two groups were subsumed as <5 % in our study. A more detailed description and exemplary tables are provided in the supplement.

2.3. Physical performance tests

Every patient received comprehensive geriatric assessment including physical performance testing. The TUG was evaluated as the time a patient needed to get up from a chair in seated position, walk to a line three meters away, turn 180°, walk back and sit back down [11]. Muscle strength was evaluated based on the handgrip strength using the validated handheld hydraulic dynamometer (JAMAR, Los Angeles, CA) [12]. The patient was positioned in a sitting position with their shoulders adduced, elbows flexed to 90°, the forearms in a neutral position and wrist between 0 and 30° of dorsiflexion holding the dynamometer [13]. Alternating from right to left three measures were taken from each side and the highest value was reported and used for further diagnosis and analysis. During the measurement the patient was encouraged by the therapists to increase the grip strength. Between each measurement only the time to change the dynamometer from one hand to the other was permitted as a pause. The gait speed was determined as the time a patient needed to walk 4 m. Each patient was granted two trials of which the better time was used for the calculation of the 4 m speed in seconds per meters (m/s). During the test the patients were allowed to wear their own shoes and use their usual auxiliary means. Patients were instructed to walk at their normal speed and no acceleration or deceleration phase was integrated. For the chair rise test (CRT) we measured the time a patient needed to get up five times from a sitting position without using their arms. Short Physical Performance Battery (SPPB) score was calculated from 4-m gait speed, chair rise test and balance test. In each category patients were assigned 0–4 points depending on the level of performance. Patients received 0 points when they were either "unable to perform" the category or the investigator or patient felt it was unsafe for the patient to try. Summing the three categories a score range from 0 to 12 resulted, with higher scores indicating better physical performance [14].

2.4. Further variables

During the geriatric assessment we assessed the bodyweight measured in kilogram (kg) and body height measured in centimeters (cm) and calculated the body mass index (BMI) as the bodyweight in kg divided by the squared body height in meters (kg/m^2). Sarcopenia or probable sarcopenia was assessed according to the EWGSOP2 criteria as defined by a reduction in grip strength (probable sarcopenia, women <16 kg, men <27 kg) and an appendicular skeletal muscle index (ASMI) as measured by the Dual Energy X-Ray (DXA) lower than 5.50 kg/m^2 in women and 7.0 kg/m^2 in men (sarcopenia) [15]. The T-Score and bone mineral density (BMD) was also assessed by DXA measurement. The hip fracture risk according to the FRAX, including the femoral T-score, if available, was calculated using the German version of the FRAX accessible online (frax.shef.ac.uk/frax/tool.aspx?lang=de) [7]. Pre-existing hip- and vertebral fractures and the number of falls were extracted from our database. The activities of daily living were assessed using the Barthel index [16]. The cognitive status was assessed by the German version of the mini mental state examination (MMSE) [17,18]. For the assessment of the nutritional status we used the short version of the mini nutritional assessment (MNA-SF) [19]. The total number of diagnoses and medications as well as the diagnosis of osteoporosis and the intake of specific anti-osteoporotic medication were taken from the doctor's report.

2.5. Statistical analysis

Continuous variables were expressed as mean and standard deviation, categorial variables as number and percentage. Group differences were evaluated by ANOVA for metric data and by Chi-square-test for dichotomous data.

After adjustment for potential confounders (BMI, age, sex) the associations of group allocation to the 5–10 % and the >10 % fracture risk group in comparison to the <5 % group with ADL, number of regularly taken medications, handgrip strength, chair rise test, gaitspeed, SPPB total score, and MNA-SF were analyzed using logistic regression analysis and presented as Odds Ratios with 95 %-confidence intervals. Overall, significance was assumed when $p \leq 0.05$. All analyses were performed using SPSS version 29.

2.6. Ethics

Written informed consent was obtained from all patients before inclusion in the registry. Ethical approval for the MUSAR registry (vote no 17–874) and the current study (vote no 24–0071) have been granted by the ethics committee of the Medical Faculty of the LMU Munich.

3. Results

3.1. Baseline characteristics

Table 1 shows the baseline characteristics of the total study population and stratified for the risk-groups. 34 (21 %) of the included 166 patients were allocated to the low−/moderate risk group. 40 (24 %) patients were allocated to the high-risk and the majority of the patients (n = 92 (55 %)) was allocated to the very high-risk group. The mean age of the total study population was 82 ± 6 years. Patients allocated to the

Table 1
Baseline characteristics of patients.

Characteristics	Total n = 166	0- < 5 % fracture risk	5–10 % fracture risk	>10 % fracture risk	p value*
n (%)	166 (100)	34 (21)	40 (24)	92 (55)	
Age [years]	82 (6)	79 (5)	81 (5)	83 (5)	<0.001#
Female n (%)	120 (100)	19 (16)	26 (22)	75 (62)	0.008°
BMI [kg/m^2]	27 (5)	30.6 (5.7)	27.2 (5.0)	24.9 (4.7)	<0.001#
Probable sarcopenia or Sarcopenia[1] n (%)	63 (100)	8 (13)	12 (19)	43 (68)	0,028°
ASMI[a] [kg/m^2]	6.8 (1.3)	7.6 (1.4)	7.0 (1.0)	6.4 (1.1)	<0.001#
T-Score[2]	−1.4 (1.3)	0.1 (0.9)	−0.8 (0.8)	−2.3 (0.8)	<0,001#
BMD[b,3] hip [g/cm^2]	0.86 (0.17)	1.05 (0.11)	0.92 (0.10)	0.74 (0.11)	<0.001#
Mean FRAX hip fracture risk [%]	8 (10)	2 (2)	4 (4)	12 (12)	<0.001#
Number of patients meeting the ≥ 3 % 10-year hip fracture risk according to FRAX n (%)	111 (100)	6 (5)	19 (17)	86 (78)	<0.001°
Pre-Existing vertebral fracture n (%)	45 (100)	4 (9)	8 (18)	33 (73)	0.013°
Pre-Existing hip fracture n (%)	15 (100)	0 (0)	4 (27)	11 (73)	0.112°
Number of patients with at least one fall[4] n (%)	84 (100)	9 (11)	18 (21)	57 (68)	< 0.001°
ADL	92 (10)	95 (9)	92 (11)	91 (10)	0.076#
MMSE	28 (2)	28 (2)	28 (2)	27 (2)	0.103#
No. medications	9 (4)	8 (4)	9 (4)	9 (3)	0.123#
No. diagnoses	8 (3)	8 (2)	9 (3)	8 (3)	0.403#
No. risk-factors	5 (3)	3 (3)	5 (3)	6 (2)	<0.001#
Grip strength [kg]	22 (9)	28 (10)	24 (9)	19 (7)	<0.001#
Chair rise test [s]	19 (9)	16 (6)	18 (7)	21 (10)	0.029#
Gait speed [m/s]	0.9 (0.5)	1.2 (0.6)	0.8 (0.3)	0.8 (0.5)	<0.001#
SPPB	7 (3)	9 (3)	7 (3)	7 (3)	0.005#
MNA	11 (3)	13 (1)	11 (2)	11 (3)	<0.001#

All measures are presented as mean ± SD unless otherwise noted.
#: ANOVA.
°: Chi-square-test.
[1] n: 164.
[2] n: 140.
[3] n: 134.
[4] n: 163.
[a] : Appendicular skeletal muscle lean mass index.
[b] : Bone Mineral Density.

very high-risk group were significantly older (83 years ±5) than those in the high-risk (81 years ±5) and low−/moderate-risk group (79 years ±5, p ⟨0,001). Most of the study population (n = 120 (72 %)) was female. Also, most of the included women were allocated to the very high-risk group (62 %, high-risk: 22 %, low−/moderate-risk: 16 %, p = 0,008). Patients in the very high-risk group significantly suffered more often from sarcopenia or probable sarcopenia (68 %, high-risk: 19 %, low−/moderate-risk: 13 %, p = 0.028) and had a lower appendicular skeletal muscle mass index (ASMI) (6.4 kg/m^2 ± 1.1, high-risk: 7.0 kg/m^2 ± 1.0, low−/moderate-risk: 7.6 kg/m^2 ± 1.4, p < 0.001). Also, the femoral T-score and the bone mineral density (BMD) was lowest in the very high-risk group (T-Score: very high-risk: −2.3 ± 0.8, high-risk: −0.8 ± 0.8, low−/moderate-risk: 0.1 ± 0.9, BMD: very high-risk: 0.74 ± 0.11, high-risk: 0.92 ± 0.10, low−/moderate-risk: 1.05 ± 0.11, p < 0.001). The hip fracture risk according to the FRAX was highest in the very high-risk group (12 % ± 12, high-risk: 4 % ± 4, low−/moderate-risk: 2 % ± 2, p < 0.001). From all patients allocated to the very high-risk group 86 from 92 patients met the therapeutic threshold according to the FRAX hip fracture risk (≥3 % 10-year fracture risk) [20], in the high-risk group 19 from 40 patients and in the low−/moderate-risk group 6 from 34 patients. From all patients who had suffered a vertebral fracture or a hip fracture before the majority was allocated to the very high-risk group but statistical significance was only reached for patients with a vertebral fracture. From all patients who fell at least once the majority was allocated to the very high-risk group.

For the mini mental state examination, the total count of regularly taken medications and total number of diagnoses no statistically significant differences between the groups could be identified. With regard to the number of risk factors in the very high-risk group significantly more risk factors were present (6 ± 2) than in the high-risk (5 ± 3) and the low−/moderate-risk group (3 ± 3, p < 0,001). A description of the three most frequent risk factors for each fracture-risk group can be found in the supplement (supplement table 3). The patients in the very high-risk group performed significantly worse in all physical performance tests (handgrip strength, chair rise test, gait speed, SPPB) than those allocated to the high-risk or low−/moderate-risk group. For the living situation and marital status no significant differences between the groups were found.

3.2. Logistic regression analysis

Table 2 shows the results of the logistic regression analysis. ADL, the number of regularly taken medications, the handgrip strength, the gait speed, the total SPPB score and the MNA-SF score showed significant associations with the group allocation to the very high-risk group throughout all models. For the group allocation to the high-risk group the gait speed, total SPPB score and the MNA also showed significant associations throughout all models.

4. Discussion

As the majority of patients was allocated to the high-risk or very high-risk group geriatric patients were demonstrated to be at a striking risk for osteoporosis and fractures. Since poor performance in geriatric assessment, malnutrition and polypharmacy were present in very high-risk patients this group seems to be very vulnerable. Moreover, bone anabolic treatment will gain significance in anti-osteoporotic therapy so its feasibility for daily clinical practice has to be addressed.

4.1. Distribution of the fracture risk groups

Approximately 80 % of the study population was found to have a severe fracture risk for the next three years with a concomitant indication for specific anti-osteoporotic treatment. The FRAX also identified the majority of patients as therapy requiring according to their 10-year hip fracture risk of ≥3 % [20].

With regard to the emerging very high-risk classification, according to the German guideline, >50 % of the study population were identified to be at very high-risk for a fracture within the following three years for which bone anabolic treatment is recommended [1]. Especially in geriatric patients clinicians therefore will have to familiarize with this new treatment option and feasibility for daily clinical practice [21–23].

In addition, even though only the two highest risk factors may be used for calculating fracture risk, especially in the high-risk and very high-risk group, a larger number of risk factors were present indicating that the actual fracture risk might be even higher than 10 % in many of these patients.

Also, especially in aged women the risk is striking as >80 % of the female study population fell into to the therapy-requiring risk-groups with the majority (>60 %) being classified as very high-risk patients.

Table 2
Results from logistic regression analysis.

Independent variable	Dependent variable	
	5–10 % vs. <5 % fracture risk	>10 % vs. <5 % fracture risk
	Odds ratio (95 % confidence interval)	
Handgrip strength		
Model 1	0,954 (0,907-1,004)	**0,888 (0,840-0,938)***
Model 2	0,954 (0,905-1,005)	**0,875 (0,817-0,937)***
Model 3	0,958 (0,908-1,011)	**0,880 (0,817-0,947)***
Model 4	0,949 (0,884-1,018)	**0,880 (0,802-0,965)***
Chair rise test		
Model 1	1,057 (0,973-1,149)	**1,083 (1,011-1,159)***
Model 2	1,080 (0,987-1,181)	**1,105 (1,020-1,198)***
Model 3	1,077 (0,983-1,180)	1,076 (0,991-1,168)
Model 4	1,072 (0,978-1,177)	**1,088 (1,004-1,179)***
Gaitspeed		
Model 1	**0,134 (0,037-0,490)***	**0,318 (0,141-0,715)***
Model 2	**0,059 (0,011-0,321)***	**0,265 (0,111-0,632)***
Model 3	**0,058 (0,010-0,335)***	**0,356 (0,161-0,787)***
Model 4	**0,058 (0,010-0,335)***	**0,291 (0,123-0,688)***
SPPB total score		
Model 1	**0,820 (0,677-0,994)***	**0,757 (0,634-0,903)***
Model 2	**0,769 (0,617-0,959)***	**0,693 (0,550-0,874)***
Model 3	**0,778 (0,622-0,974)***	**0,711 (0,552-0,916)***
Model 4	**0,775 (0,619-0,970)***	**0,687 (0,524-0,901)***
ADL		
Model 1	0,968 (0,918-1,020)	**0,940 (0,890-0,993)***
Model 2	**0,912 (0,842-0,987)***	**0,880 (0,817-0,949)***
Model 3	**0,914 (0,843-0,991)***	**0,897 (0,831-0,967)***
Model 4	**0,917 (0,845-0,995)***	**0,909 (0,845-0,979)***
MNA-SF		
Model 1	**0,640 (0,468-0,875)***	**0,531 (0,385-0,731)***
Model 2	**0,674 (0,486-0,934)***	**0,630 (0,447-0,886)***
Model 3	**0,667 (0,478-0,932)***	**0,683 (0,479-0,973)***
Model 4	**0,662 (0,472-0,929)***	**0,652 (0,441-0,963)***
No. medications		
Model 1	1,077 (0,953-1,218)	**1,147 (1,011-1,302)***
Model 2	**1,156 (1,007-1,328)***	**1,293 (1,108-1,509)***
Model 3	1,140 (0,989-1,313)	**1,270 (1,077-1,497)***
Model 4	1,156 (0,997-1,341)	**1,378 (1,131-1,677)***

Model 1: crude model.
Model 2: adjusted for BMI.
Model 3: adjusted for BMI, age.
Model 4: adjusted for BMI, age, sex.
* : $p \leq 0{,}05$.

Taken together, a strong association between osteoporosis and the concomitant increased fracture-risk in geriatric patients could thus be shown highlighting the urgent need for initiation of specific treatment [24].

4.2. Associations with geriatric assessment

Overall, patients allocated to the high-risk or very high-risk group showed more limitations in all physical performance tests (handgrip strength, chair rise test, gaitspeed, SPPB) than those in the low−/moderate risk group. Even though not statistically significant but in line with these findings also the total score of ADLs tended to decrease with increasing fracture risk representing an enhanced need for assistance in higher fracture-risk groups [25]. Of note, as this study was conducted in relatively healthy community-dwelling patients ADLs still ranged in the upper limit even in the high-risk and very high-risk groups indicating the patients sustained activity level which on the other hand might favor falls and fractures. Additionally, both the high-risk and the very high-risk group were demonstrated to be at risk for malnutrition and suffering from polypharmacy. For all these reasons patients with osteoporosis/an increased fracture risk seem to be vulnerable and therefore need conscientious examination and timely therapy planning.

Additionally, our results identified significant associations between limitations in muscle power and function and an increased fracture risk. Especially a decreased gait speed and poor performance in the SPPB were thoroughly associated with a severe fracture risk whereas handgrip strength and chair rise test only showed associations with the very high fracture risk group. This was interesting as a recent review by Vendrami et al. demonstrated ambivalent results for muscle power and function parameters with regard to the fragility fracture risk but recommended handgrip strength and gait speed as the best parameters especially as they are easy to assess in daily clinical practice and showed acceptable results with regard to the fracture risk [26]. Nevertheless, physical performance parameters seem to be important indicators for fractures so that inclusion of the TUG as one of the risk factors in the recent guidelines seems highly reasonable [1,26]. In line with these findings, we also found a higher ability to perform ADLs and a normal nutritional status to be protective factors for a severe fracture risk [27,28]. By its association with loss of muscle power and function, malnutrition is also a crucial risk factor for falls and subsequent fractures [29]. Therefore, malnutrition assessment has been suggested as an important part of fall risk assessment in order to identify high-risk patients [30]. Fang et al. for example found a very good diagnostic capability for recognizing major osteoporotic fractures for the MNA-SF [27]. Along with our findings the MNA-SF therefore might be an easily accessible tool for timely overall fracture risk identification [27,31].

As polypharmacy is a striking issue among many geriatric patients [32] also the number of medications was associated with a very high fracture risk in our study [33]. Because of all these findings high-risk and very high-risk patients are in pressing need for assessment and improvement of physical function, nutritional intervention strategies and medication management [26,27,33].

5. Strengths and limitations

This study was conducted on a relatively small sample, which may limit the generalizability of the findings for the broader population. However, as numerous variables need to be considered our cohort offers a well characterized collective of geriatric patients. Therefore, fracture risk calculation could be based on all risk factors, including the results from bone mineral density measurement, according to the latest German guideline. Of note, our results may be influenced as 63 of the included patients were diagnosed with either probable or confirmed sarcopenia, a condition that has itself been associated with a high fracture risk. Additionally, as this study included relatively healthy community-dwelling patients results might be different in patients with a higher burden of disease. As even in a healthy cohort an extensive number of patients was identified as being at high-risk or very high-risk for a fracture within the next three years the percentage might be even higher in cohorts with more severe health conditions. Also, due to the relatively healthy study cohort mean values of all observed variables were comparatively high so that for example we were only able to demonstrate a tendency of a decrease in ADLs with increasing fracture risk but no statistically significant result. Generally, longitudinal data would be of interest in order to confirm our findings. Even though our registry was found in 2018 no sufficient number of patients could be included for longitudinal analysis as the enrollment happened gradually and not at a single point of time. Nevertheless, this study provided valuable information on the high number of geriatric patients in need for specific anti-osteoporotic treatment and improvement of its supply.

6. Conclusion

The majority of the geriatric patients is at a high- or very-high fracture risk and in need of specific anti-osteoporotic treatment. Especially patients in the very high-risk group were identified as being extremely vulnerable as they showed severe limitations in physical-function, ADLs and also suffered from malnutrition and poly-pharmacy. Therefore, further studies investigating other parameters from geriatric assessment are needed. Our findings highlight the urgent need for clinicians to initiate risk assessment and familiarize with new therapeutic options for osteoporosis treatment in geriatric patients.

CRediT authorship contribution statement

Michaela Rippl: Writing – original draft, Visualization, Investigation, Formal analysis, Data curation. **Pauline Grupp:** Writing – review & editing, Investigation, Formal analysis. **Sebastian Martini:** Writing – review & editing, Resources, Data curation. **Katharina Müller:** Writing – review & editing, Formal analysis, Data curation. **Olivia Tausendfreund:** Writing – review & editing, Data curation. **Ralf Schmidmaier:** Writing – review & editing, Project administration, Conceptualization. **Michael Drey:** Writing – review & editing, Resources, Project administration, Formal analysis, Conceptualization.

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Declaration of competing interest

M.D. and R.S. participated in the design of the current S3 guideline on osteoporosis. All other authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bone.2024.117366.

Data availability

The data that has been used is confidential.

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