RELATIONSHIP BETWEEN VITAMIN D SUPPLY AND HEALING IN PATIENTS WITH HIP FRACTURE

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BACKGROUND:
Vitamin D (VD) deficiency is important risk factor of fractures. Yet, the relation of serum 25-hydroxyvitamin D (25OHD) levels and recovery after fractures is poorly studied.

AIMS:
To investigate the VD supply in hip fractures also with regard to lifestyle and other clinical (malignancy, kidney and liver disease, osteoporosis) conditions.
To examine vitamin-D supply on the base of preoperative t-25OHD, bioavailable (Bio-25OHD) and free (f-25OHD) vitamin-D levels and its relations to parathyroid hormone (PTHi) and calcium (Ca) concentrations in patients with hip fractures (HF).
To investigate the relation between survivorship and vitamin D supply.

PATIENTS:
202 patients (67 men, 135 women) with hip fracture (age 75±12 years) and 102 persons –matched by gender and age– with active lifestyle as control were evaluated.

<table>
<thead>
<tr>
<th></th>
<th>Female N (%)</th>
<th>Men N (%)</th>
<th>P</th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>above</td>
<td>71 (53%)</td>
<td>24 (36%)</td>
<td>0.009</td>
<td>95 (47%)</td>
<td></td>
</tr>
<tr>
<td>expected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>average</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>67 (50%)</td>
<td>36 (54%)</td>
<td>-</td>
<td>103 (51%)</td>
<td></td>
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<tr>
<td>active</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>lifestyle.</td>
<td></td>
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<tr>
<td>liver</td>
<td>7 (5%)</td>
<td>10 (15%)</td>
<td>0.019</td>
<td>17 (8%)</td>
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</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>kidney</td>
<td>21 (16%)</td>
<td>5 (8%)</td>
<td>-</td>
<td>26 (13%)</td>
<td></td>
</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>malignancy</td>
<td>30 (22%)</td>
<td>15 (22%)</td>
<td>-</td>
<td>45 (22%)</td>
<td></td>
</tr>
<tr>
<td>disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>anticoagulant therapy</td>
<td>19 (14%)</td>
<td>11 (16%)</td>
<td>-</td>
<td>30 (15%)</td>
<td></td>
</tr>
<tr>
<td>died</td>
<td>17 (13%)</td>
<td>14 (21%)</td>
<td>-</td>
<td>31 (15%)</td>
<td></td>
</tr>
<tr>
<td>survival</td>
<td>19 (5.52 days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>time:</td>
<td></td>
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</tbody>
</table>

Table 1: The main characteristic data of hip fractured patients

MEASURED BIOCHEMICAL MARKERS:
t-25OHD (protein bindig assay, Roche), PTHi (ECLA, Cobas, Roche), DBP (Immuno-turbidimetry, Dako), albumin (colorimetry, Modular Roche), and Ca were measured. The Bio-25OHD and free-25OHD values were calculated using a mathematical model (Vermeulen et al, 1999, Bhan et al, 2012).

RESULTS:

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Occurrence of Vitamin D deficiency and secondary hyperparathyroidism on the base of active control decision limit.}
\end{figure}

Vitamin D deficiency and secondary hyperparathyroidism occurred significantly more frequently in patients with hip fracture than in the control group.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{The levels of three different 25OHD fractions PTHi and binding proteins in HF group related to control.}
\end{figure}

The differences are significant in all biomarkers.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{Relationship between the level of vitamin D fractions and PTHi}
\end{figure}

Patients with better condition after surgery showed significantly higher level of 25OHD fractions and albumin levels than patients with worse condition. The DBP levels didn't show significant relationship with the early clinical condition, but the lowest level was observed in died patients. The three 25OHD fractions were the same in all three-survival groups, but not in the case of the 5 patients who died in 1-3 weeks after surgery.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{The fractions of 25OHD levels in survived and died patients (within a half of year follow up).}
\end{figure}

31 patients who died after surgery had significantly lower 25OHD levels in all fractions than those who survived without significant difference in PTHi levels. These results were independent from most of chronic disorders.

RESULTS OF WITHIN GROUP CORRELATIONS:
The correlations between the In-total and In-Bio-25OHD levels were excellent in both groups (HF: r=0.94 and Control: r=0.96). The further significant correlations among the biomarkers are summarized in table 2.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|}
\hline
                      & Albumin Control & DBP Control & PTHi Control & Ca Control & \hline
In-t-25OHD           & 0.26            & 0.26        & -0.41        & -0.41      & 0.25          & 0.16          \\
In-Bio-25OHD         & 0.34            & 0.40        & -0.31        & -0.20      & -0.40        & -0.42        & 0.30          & 0.17          \\
In-free-25OHD        & -0.25           & -0.35       & -0.22        & -0.40      & -0.44        & 0.22          \\
\hline
\end{tabular}
\caption{Correlations among biologically related markers}
\end{table}

We observed the supposed correlation in two groups, except for between the Ca and both fractions of 25OHD. All fractions of 25(OH)D showed similar negative correlations with the PTHi levels in both groups.

CONCLUSIONS:
- The t-25OHD measurements appear sufficient to reliable assess of vitamin D supply in both groups.
- The significant negative correlations between PTHi and 25OHD emphasize that values of higher PTHi should be take into consideration in patients with vitamin D deficieny.
- The correlation between 25OHD levels and better postoperative condition confirm the importance of vitamin D3 substitution in prevention, as well as in healing, and in increased survival rate for HF.