Evaluation of a Clinical Decision Support Rule-set for Medication Adjustments in mHealth-based Heart Failure Management

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Agenda

- **Introduction:**
  - mHealth-based Heart Failure Management
  - INTENSE-HF, HF medication groups
  - Decision support rule set / algorithm

- **Methods:**
  - Analysis dataset, Analysis platform
  - Evaluation of CDSS based on performed medication adaptations

- **Results:**
  - Event episodes, medication adaptations
  - Performance based on performed medication adaptations

- **Discussion**
Introduction: mHealth-based Heart Failure Management

- mHealth monitoring
  - monitor and manage patients at home
  - motivate patients to be compliant to treatment regimens
  - enhance patient adherence to medical treatment

- signal processing & analysing
  - filtering relevant signals
  - detect upcoming adverse events early

- Feedback, Reminders, ...

- efficiently close the heart failure management loop

- Data supply

- Visualization, ...

- Therapy adjustment

Health Data Center

- clinical decision support
  - react in time with personalized adjustments
  - better control progress of the therapy

24.06.2015
Introduction: INTENSE-HF, HF medication groups

- **INtegrated TElemonitoring and NUrse Support EValuation in HEar t F ailure**
- Clinical trial conducted between 2012 and 2014 in Austria
  - Exploratory endpoint: evaluate if telemonitoring with rule-based CDSS helps physicians to adopt medication to a target medication scheme derived from the European Society of Cardiology (ESC) Heart Failure (HF) guideline

- HF guideline addresses four large medication groups of relevance for the management of systolic HF:
  - angiotensin-converting-enzyme inhibitors (ACE-I)
  - angiotensin-receptor-blockers (ARB)
  - beta-blockers (BB)
  - diuretics
Introduction: Decision support rule set / algorithm

<table>
<thead>
<tr>
<th>Rule</th>
<th>Action</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic BP &gt; 130 mmHg</td>
<td>Increase ACE-I/ARB</td>
<td>A</td>
</tr>
<tr>
<td>Systolic BP &lt; 95 mmHg</td>
<td>Decrease ACE-I/ARB</td>
<td>A</td>
</tr>
<tr>
<td>Heart rate &gt; 70 bpm</td>
<td>Increase betablocker</td>
<td>A</td>
</tr>
<tr>
<td>Heart rate &lt; 50 bpm</td>
<td>Decrease betablocker</td>
<td>A</td>
</tr>
<tr>
<td>Weight gain &gt; 2kg in 2 days</td>
<td>Increase diuretics</td>
<td>B</td>
</tr>
<tr>
<td>Weight loss &gt; 2kg in 2 days</td>
<td>Decrease diuretics</td>
<td>B</td>
</tr>
</tbody>
</table>

Type A:
- adjusting dose of HF medication for ACE-I, ARB and BB
- fired when threshold was exceeded for the 5\textsuperscript{th} in 7 consecutive days.

Type B:
- adjusting dose of diuretics, depending on body weight gain/loss, which indicate early signs of cardiac decompensation.
Methods: CDSS evaluation example (BP sys, ACE-I)

Output: CDSS suggestion
- 10 mg
- 20 mg
- 40 mg
- 20 mg
- 10 mg
- 5 mg

Reference: Physicians prescriptions
- 10 mg
- 20 mg
- 40 mg
- 20 mg
- 10 mg
- 5 mg

Result

Monitoring days

BP sys

24.06.2015
Methods: Analysis platform, Steps

- Used KNIME-workflows for processing and analysis:
  1. Extract CDSS suggestions from INTENSE-HF database
  2. Extract medication adaptations from INTENSE-HF database
  3. Normalize medications, based on mapping table, because not every medication is same effective in the same dosage
  4. Compare performed medications changes to CDSS suggestions
  5. Classify monitoring days into one of four categories based on result from step 4
  6. Calculate Sensitivity, Specificity based on result from step 5

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting Dose</th>
<th>Dosing interval</th>
<th>Target dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisoprolol</td>
<td>1.25</td>
<td>2.5 / 2.75 / 5 / 7.5</td>
<td>10</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>6.25</td>
<td>2x6.25 / 2x12.5</td>
<td>2x25</td>
</tr>
<tr>
<td>Metoprolol-Succinat (ret)</td>
<td>23.75</td>
<td>47.5 / 2x47.5 / 3x47.5</td>
<td>2x95</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>1.25</td>
<td>2.5 / 2.75 / 7.5</td>
<td>10</td>
</tr>
</tbody>
</table>
Methods: Evaluation of performance of CDSS based on performed medication adjustments

<table>
<thead>
<tr>
<th>Medication adjustment</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring days with / without medication suggestion</td>
<td>+</td>
<td>TP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>correctly identified situation</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>FN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>incorrectly rejected situation</td>
</tr>
</tbody>
</table>

e.g. TP: monitoring days, where CDSS created medication suggestion and medication change was performed by physician
Results: Patient cohort

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (male/female)</td>
<td>15 (12/3)</td>
</tr>
<tr>
<td>Monitoring duration (mean +/- standard deviation)</td>
<td>295.8 +/- 88.8 days</td>
</tr>
<tr>
<td>Monitoring days</td>
<td>4.450</td>
</tr>
<tr>
<td>Age (mean +/- standard deviation)</td>
<td>72.1 +/- 9.0 years</td>
</tr>
<tr>
<td>Medication adjustments per patient (mean +/- standard deviation)</td>
<td>5.7 +/- 5.3</td>
</tr>
<tr>
<td>CDSS suggestions per patient (mean +/- standard deviation)</td>
<td>13.0 +/- 9.4</td>
</tr>
</tbody>
</table>
Results: Evaluation of performance of CDSS based on performed medication adjustments

<table>
<thead>
<tr>
<th>Medication adjustment</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitoring days with/without medication adjustment suggestion</td>
<td>+</td>
<td>TP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>265 (5.9 %)</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>FN</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14 (0.3 %)</td>
</tr>
</tbody>
</table>

- Sensitivity = TP / (TP + FN) = 94 %
- Specificity = TN / (FP + TN) = 92 %
Conclusion

- we used rule-based CDSS to generate medication adaptations suggestions and physicians decisions as reference annotations for appropriate medication adjustment recommendations.

- Medication adaptations have been performed by the physician in reaction to CDSS suggestions

- We conclude that guideline-based CDSS did suggest indeed trigger some correct medication adaption
  - number of FP is higher than TP
  - only 15 patients included and no further data is expected, as the study has been terminated in October 2014.
Discussion

- Clinical point of view: does usage of CDSS result in a better outcome for the patients?
- Problem in determining the effectiveness of CDSS:
  - lack of reference annotations, additional annotations of the clinical courses of both the telemonitoring and the control group will be needed
- Future work:
  - exploratory endpoint of INTENSE-HF, analyze if guideline-based CDSS was able to bring telemonitoring patients closer to a guideline-based medication scheme than control group
  - elucidate how the rule-set has to be modified to increase the reliability and acceptance of CDSS systems for HF management.
Thanks!

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Results: CDSS medication suggestions, medication adaptations

<table>
<thead>
<tr>
<th>Rule</th>
<th>CDSS</th>
<th>Physician</th>
<th>CDSS = Physician</th>
<th>CDSS ≠ Physician</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE/ARB increase</td>
<td>26</td>
<td>13</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>ACE/ARB decrease</td>
<td>9</td>
<td>9</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Betablocker increase</td>
<td>81</td>
<td>17</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Betablocker decrease</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Diuretics increase</td>
<td>42</td>
<td>19</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Diuretics decrease</td>
<td>36</td>
<td>25</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Σ</td>
<td>195</td>
<td>86</td>
<td>30</td>
<td>9</td>
</tr>
</tbody>
</table>
Previous and related work

- Before INTENSE-HF, a retrospective feasibility analysis of the rules used in the CDSS was done with datasets from previous telemonitoring trials.
  - In this preceding analysis, we focused on the absolute number of events generated by the CDSS.
- Evaluation of existing literature revealed that previous work primarily analyzed user-acceptance of CDSS or described the development process of CDSS.
- To our best knowledge, up to now, there is no related study, which aimed to evaluate CDSS by using performed medication adjustments as reference annotations.