Institutional report - Cardiac general

Screening methods for delirium: early diagnosis by means of objective quantification of motor activity patterns using wrist-actigraphy

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Received 29 August 2008; received in revised form 3 November 2008; accepted 3 November 2008

Abstract

Delirium after cardiac surgery is a risk factor for adverse outcome and even death. Disturbance of motor activity is a core feature of delirium, but hypoactive delirium often remains unrecognized. We explored wrist-actigraphy as a tool to objectively quantify postoperative recovery of 24-h rest–activity patterns to improve the early recognition of delirium after surgery. Motor activity was recorded by wrist-actigraphy after cardiac surgery in 88 patients over 65 years of age. Patients were assessed daily by using the CAM-ICU. Our final analyses were based on 32 non-delirious patients and 38 patients who were delirious on the first day after surgery. The delirious patients showed lower mean activity levels during the first postoperative night (P < 0.05), reduced restlessness during the first day (P < 0.05), and a lower mean activity of the 5 h with lowest activity within the first 24 h (P = 0.01), as compared to the non-delirious patients. Already at a very early stage after cardiac surgery, a difference in motor activity was observed between patients with and without a delirium. As an unobtrusive method, actigraphy has the potential to be a screening method that may lead to early diagnosis and treatment of delirium.

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Keywords: Delirium; Postcardiotomy; Actigraphy; Motor activity; Motor subtypes

1. Introduction

Delirium after surgery, particularly in elderly patients, is an independent risk factor for adverse outcome and even death [1]. It is unfortunate that it is still poorly recognized, especially the hypoactive subtype [2]. Complex issues are involved in relation to validity of diagnostic tools [3]. The most frequently used diagnostic tools for delirium, the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) [4] and the Delirium Rating Scale – Revised ’98 (DRS-R98) [5], may improve detection, but require training and can provide ambiguous results. In addition, prophylactic use of haloperidol has been shown to reduce the severity and duration of delirium in geriatric patients [6]. However, although prophylactic use of haloperidol may improve outcome in general, it leads to unnecessary treatment of 68–77% of the elderly patients after cardiac surgery [7, 8]. An objective and easy to use tool for the early detection of delirium is desirable.

∗Presented at the 22nd Annual Meeting of the European Association for Cardio-thoracic Surgery, Lisbon, Portugal, September 14–17, 2008.
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Considering the clinical importance of disturbed motor activity patterns in a delirium after cardiac surgery, quantification of motor activity patterns seems an obvious choice. Wrist-actigraphy can be used as an objective method to assess 24-h patterns of spontaneous motor activity for prolonged periods of time. The method accurately distinguishes rest from activity periods in a valid and reliable way [9]. In a variety of psychiatric and neurological patient categories, wrist-actigraphy has been used to quantify disturbances in sleep–wake schedule, alterations in diurnal rest–activity patterns, as well as psychomotor disturbances (psychomotor retardation or agitation) [e.g. 10].

We explored the usefulness of wrist-actigraphy to improve the early recognition of delirium after surgery by focusing on the (circadian) motor activity patterns during the first night and day following cardiac surgery.

2. Materials and methods

2.1. Subjects

We studied 88 patients of 65 years and older who underwent elective cardiac surgery at the department of Cardiothoracic Surgery of the Erasmus Medical Center. Patients were excluded from the study if they required emergency surgery, showed signs of pre-existing delirium, or were...
unable to speak sufficient Dutch or could not provide written informed consent. In addition, subjects were excluded if they were comatose on day 1 \((n=5)\) or diagnostic assessments could not be made \((n=6)\). Due to technical problems with the actigraph \((n=5)\) or sudden discharge from the hospital \((n=2)\), the data of another seven patients were lost for evaluation. As such, 70 subjects were included in our analyses.

The study protocol was approved by the Medical Ethical Committee of the Erasmus MC and conducted in accordance with the criteria of Good Clinical Practice (Declaration of Helsinki, 2004).

2.2. Procedure

The patients underwent elective cardiac surgery (coronary artery bypass graft, valve surgery, or both) at the department of Cardiothoracic Surgery of the Erasmus Medical Center in Rotterdam. Eligible patients were invited to participate in the study after having received detailed information in both oral and written form. All patients provided written informed consent before entering the study.

Surgery was scheduled at variable times during the day; however, most patients were operated on during the morning. As soon as the patients returned from surgery to the intensive care unit (usually in the afternoon; day 0), the actigraph was placed on the non-dominant wrist for continuous measurement of 24-h motor activity patterns.

The data presented in this study are limited to the first postoperative night and day. Daily, between 09.00 and 12.00 h, the diagnosis delirium was assessed and evaluated by a senior psychiatrist and/or trained researchers based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [11] and the four-item diagnostic Confusion Assessment Method-Intensive Care Unit (CAM-ICU) algorithm. A positive diagnosis requires the presence of an acute onset and fluctuating course, as well as inattention, and either disorganized thinking or altered level of consciousness [4]. We used the CAM-ICU score of the first day to define our subgroups of delirious and non-delirious patients.

If the patients developed a delirium, standardized psychiatric treatment according to APA guidelines was applied in all delirious patients [12]. Each day, details of the medical condition, including body fixation, and possible adverse reactions of the patients towards the use of the actigraph were recorded in separate files.

2.3. Wrist-actigraphy

To assess spontaneous 24-h motor activity, the patients wore a wrist-actigraph continuously for six days on the non-dominant wrist. The non-dominant wrist is more reflective of movements of the total trunk and less of movements involved in performing specific tasks [9].

The Activwatch® actigraph (Cambridge Neurotechnology Ltd, Cambridge, UK) \((\text{size } 27 \times 26 \times 9 \text{ mm}; \text{weight } 16 \text{ g})\) contains a piezo-electric acceleration sensor and counts the number of supra threshold movements \((>0.05 \text{ g acceleration})\) per 1 min epochs lengths. The following motor activity parameters were computed per nighttime \((23.00 \text{ h}–06.00 \text{ h})\) and daytime period \((06.00 \text{ h}–23.00 \text{ h})\: mean Activity per minute (the average activity score in those 1 min epochs where scores of \(>0\) were recorded); number of minutes Immobile (the total number of minutes where a score of zero was recorded); and Restlessness Index (the addition of the percentage of time spent moving and the percentage immobility phases of 1 min). In addition, the mean activity of the 5 h with the least activity (L5) and the 10 h (M10) with the highest activity within the first 24-h period were analyzed to evaluate more sustained periods of (in)activity independent of clock-time, reflecting circadian rhythm disturbances [10].

2.4. Statistical methods

Differences between the surgical characteristics of the delirious and non-delirious patients were evaluated by means of \(t\)-tests, with the exception of lowest body temperature (Mann–Whitney \(U\)-test, due to skewness of the distribution). The activity parameters during the first postoperative night and day period were all not normally distributed (Kolmogorov–Smirnov tests). Therefore, data are presented in median (minimum, maximum) values; Mann–Whitney \(U\)-tests were performed to evaluate differences between delirious and non-delirious patient groups. All analyses were performed with SPSS for Windows (version 16.0). A \(P<0.05\) was used to indicate a significant difference.

3. Results

3.1. Patient and operation characteristics

The percentage of males and females was similar for both groups, whereas mean age was significantly higher for the delirious patient group as compared with the non-delirious patient group \((\text{Table 1})\).

With the exception of mitral valve plasties in combination with coronary artery bypass graft surgery and Bentall procedures (which were more common in the delirious group), the types of surgery were overall equally distributed between the two groups.

The duration of the surgery and the extra corporal circulation were significantly longer in the delirious group as compared to the non-delirious group \((\text{Table 1})\). The duration of aorta cross-clamp time showed a trend \((P=0.06)\) towards a significant increase in the delirious patients. The lowest body temperature during surgery was also not significantly different between the delirious and non-delirious groups.

3.2. Illustrative actigraphy examples

Fig. 1 illustrates individual actigraphy characteristics of post-surgery recovery of 24-h motor activity patterns in a non-delirious patient \((\text{Fig. 1a})\) and a delirious patient \((\text{Fig. 1b})\). A gradual recovery of 24-h rest–activity periodicity was usually apparent in the non-delirious patients. In the severe delirious patients, recovery of rest–activity patterns was less apparent.
Table 1
Demographic and surgical characteristics of non-delirious and delirious patients

<table>
<thead>
<tr>
<th></th>
<th>Non-delirious</th>
<th>Delirious</th>
<th>T/Z-value; P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>32</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Gender, males/females</td>
<td>16/16</td>
<td>19/19</td>
<td></td>
</tr>
<tr>
<td>Age in years mean</td>
<td>73.0 (4.6)</td>
<td>76.0 (4.9)</td>
<td>–2.56; 0.01</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>12 (38%)</td>
<td>13 (34%)</td>
<td></td>
</tr>
<tr>
<td>AVR</td>
<td>10 (31%)</td>
<td>8 (21%)†</td>
<td></td>
</tr>
<tr>
<td>AVR + CABG</td>
<td>5 (16%)</td>
<td>7 (18%)**</td>
<td></td>
</tr>
<tr>
<td>MVP</td>
<td>3 (9%)</td>
<td>4 (11%)</td>
<td></td>
</tr>
<tr>
<td>MVP + CABG</td>
<td>1 (3%)</td>
<td>4 (11%)</td>
<td></td>
</tr>
<tr>
<td>AVR + MVP (+ CABG)</td>
<td>1 (3%)†</td>
<td>2 (13%)†</td>
<td></td>
</tr>
<tr>
<td>Duration surgery (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>260 (63)</td>
<td>310 (93)</td>
<td>–2.63; 0.01</td>
</tr>
<tr>
<td>ECC time (min)</td>
<td>134 (44)</td>
<td>163 (61)</td>
<td>–2.17; 0.03</td>
</tr>
<tr>
<td>AoX time (min)</td>
<td>89 (34)</td>
<td>107 (43)</td>
<td>–1.95; 0.06</td>
</tr>
<tr>
<td>Lowest body temperature</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (S.D.)</td>
<td>30.9 (1.5)</td>
<td>29.8 (3.3)</td>
<td>–1.13; ns</td>
</tr>
</tbody>
</table>

AVR, aorta valve replacement; CABG, coronary artery bypass graft; MVP, mitral valve plasty; ECC time, extra corporal circulation time; AoX time, aorta cross-clamp time.

*Including 2 Bentall procedures; **Including 1 Bentall procedure; †Including 1 tricuspid valve annuloplasty; AVR + MVP; AVR + MVP + CABG, including 1 tricuspid valve annuloplasty; ns, non-significant.

Fig. 1. Examples of wrist-actigraphy recordings (based on 1 min epoch lengths) during a post-surgery recovery period of six days of a non-delirious patient (a) and a delirious patient (b). Each line indicates a 24-h period, starting at midnight. The black bars mark the analyses periods for the nights (23.00 h–06.00 h). The recordings started at 21.00 h (a) and 18.00 h (b), respectively. Daytime naps between 13.00 and 14.00 h are apparent in the non-delirious patient.

3.3. Motor activity during first postoperative night and day

The delirious patients showed a significantly lower mean activity level during the first postoperative night, and a significantly reduced restlessness during the first postoperative day, in comparison with the non-delirious patient group (Table 2). Also, the mean activity of the 5-h period with lowest activity within the first 24 h was significantly lower in the delirious patients as compared to the non-delirious patients (Table 2). Two trend-effects were observed regarding motor activity during the day-period: the number of immobility minutes was higher and mean activity level was lower for the delirious group as compared to the non-delirious group (P=0.09 and P=0.08, respectively).

Body fixation (chest and wrist fixation) did not occur in the non-delirious group, and was applied twice for a short period of time in two patients of the delirious group during the first postoperative day to prevent self-harm.

4. Discussion

Our data illustrate that at a very early stage after cardiac surgery, a difference in behaviour can be measured between patients with and without delirium. The delirious patients showed lower mean activity levels during the first postoperative night, and a reduced restlessness during the first day, compared to non-delirious patients.

Wrist-actigraphy was well tolerated by all patients. In comparison with other techniques to objectively measure movement, such as video monitoring and more complex
accelerometry techniques, wrist-actigraphy is easy to use and has little influence on the privacy of the patients.

Increased or decreased psychomotor activity and a disturbed sleep–wake cycle are among the key symptoms of delirium [13]. A distinction is usually made between hyperactive, hypoactive or mixed subtypes of delirium, with presumed differences in underlying pathophysiology and response to treatment [3]. The hypoactive subtype of delirium is usually poorly recognized, partly because the clinical ratings emphasize isolated incidences of (night-time) restlessness or uncontrollable behavior (because they draw the attention of clinicians and nurses). Changes in the circadian rhythm are among the most often present symptoms in delirium [11]. Our preliminary data show that reduced motor activity may be a much more prevalent feature of delirium than presently assumed, at least during the first postoperative night and day.

Possible limitations of this study are that the results may reflect the characteristics of our elderly patient group (based on DRS-R98 analyses, the majority of patients were hypoactive, 53%, or mixed, 35%). Parts of the results may be due to the administration or persistent effects of opiates and sedatives during this initial postoperative period. Also, the standardized treatment of a delirium with haloperidol may have influenced our measurements, although no significant changes on actigraphic measures were found in a study using comparable doses of haloperidol in healthy volunteers [14].

This study focused on early recognition of delirium; we used the CAM-ICU records of the first day after surgery to attribute the patients to either the delirious or non-delirious group. As a consequence, the group of delirious patients contained patients with durations ranging from one to more days. Because a delirium is an indicator of underlying serious problems and is associated with severe complications, there is clinical support for this choice.

In agreement with other authors, we found that longer duration and higher complexity of surgery were associated with a higher chance of experiencing a delirium after cardiac surgery [e.g. 8]. Further research should clarify to which extent processes such as micro-emboli, inflammatory processes (e.g. cytokine activation) or arteriosclerotic changes in the brain, preexisting psychiatric or neurological disorders, genetic influences, differences in specific surgical (such as deep-cooling) or anesthetic techniques, drug use or other frailty factors contribute to the measured motor differences between the two groups.

Variability of all our motor activity parameters was high in both groups of elderly patients, but particularly in the delirious group, reflecting potential influences of age, pre-surgery activity level and physical condition, as well as daily fluctuations in severity of illness, medical complications and medication use, body fixation, and the presence of drains or intubation. A larger study is necessary to unravel the contribution of each of these factors to recovery of motor activity patterns, in relation to the presence of a delirium. In such a study, the potential of the method to actually predict delirium should also be addressed, to evaluate the possibility to obtain clear cut-off points beyond which the risk of delirium would justify prophylactic treatment in specific patients.

5. Conclusion

Disturbance of motor activity patterns is an important clinical manifestation of a delirium after cardiac surgery. Our data show that already at a very early stage after cardiac surgery, a difference in motor activity was observed between patients with and without a delirium. As an unobtrusive method, actigraphy has the potential to be a screening method that may lead to early diagnosis and treatment of delirium.

Acknowledgments

We thank E.A.J. Berenschot-Huijbregts, B.A. Bogers, E. van ‘t Hof, N. Heijmeskamp and H. Rehorst for their assistance in the data collection.

References


Conference discussion

Mr. T. Treasure (London, United Kingdom): I am a cardiothoracic surgeon and I have researched in this area in the past over many years, and I guess that is why I was asked to come and discuss it. First of all, I would like to say how much I appreciate two things: one, as a psychiatrist you apply your skills to help us solve one of these problems and, the other, that you come and talk to us about it yourself.

I did animal work on this problem and worked with a neuroscientist, and when I started clinical work we put together a team which included a psychiatrist, a psychologist, and a neurologist with a special interest. The first point I would like to make is that with any of these questions that affect us in cardiac surgery, by teaming up with other disciplines we will learn so much more. All too often I see juniors doing projects based in other disciplines such as haematology or neurology for example, and they lack the background knowledge to really get the best out of it. So I would like to say that first.

Now, the other thing that I would also like to reflect on was the early days of us doing research. For example, in Torkel Aberg's study, he performed lumbar puncture, taking out CSF and measuring adenylate kinase; far too invasive for research and too difficult. On the other hand, we used batteries of neuropsychological tests which were also difficult in that there were many other factors in play. So your method is very attractive. So my first question is, to what extent do you think that this non-invasive, reproducible measurement reflects the sort of injury to the brain that concerns us during the course of cardiopulmonary bypass and circulatory arrest?

That leads on to my next question: if it is a good, reliable surrogate, would it be a good tool to use in researching one protective strategy versus another?

The third question concerns specialist vocabulary. The word ‘delirium’ is used from the early days in American literature. As a native English speaker and doctor, I find it a rather archaic term. It does at least have the advantage that it isn’t a very precise diagnosis, but it is a funny old word, delirium, and I am rather interested that you still use it. I would like you to comment on whether you think, as a psychiatrist, it has the level of diagnostic precision that would help us as cardiac surgeons to relate it to what goes wrong with the brain after bypass, or you may even think that the lack of diagnostic precision leaves you open to say ‘I don’t need to be precise about this – the brain isn’t working very well at this stage – that is as much as I can say’. Do you see what I mean? I would like your advice on it, really, but I come from a position of thinking, that’s a bit old fashioned.

Dr. Osse: Well, deliria really means out of the track, out of the trail. In fact, it is not very precise, but the problem is we don’t have very precise details about brain function in living persons. Just recently we were able to approach the brain of a living person in a manner which a normal person would allow, like functional MRI. So I am happy that there is some progress in psychiatry.

From a clinical point of view, the delirium diagnosis really makes sense. In European psychiatry, delirium is a consciousness disorder with a problem in consciousness, whereas in American psychiatry, the diagnosis is not defined in that way. When we have a consciousness disorder and we see a patient, we can say there is something in the bodily function going wrong. So if somebody is falling asleep while we assess them, that is really a big argument to find out if the bodily function isn’t working properly, and that is fitted in the diagnosis of delirium. So it isn’t a very good diagnosis, but for the moment it is rather clinically relevant.

Movements in delirium are an interesting point, for it is the way delirium are defined. You have the so-called subtypes of hyperkinetic and mixed delirium. So that is a reason to look at movement, for there is some argument that the hyperkinetic delirium might need another strategy, but in fact these strategies have not been formulated yet.

Dr. M. Kolowca (Rzeszow, Poland): Don’t you think that your results of your study are biased by drugs? Did you check if there was any difference between these two groups, delirium and non-delirium, with drugs, like morphine, like sedative drugs?

Dr. Osse: No, we didn’t research that in this group. We are doing it in the next group. There is also an ethical problem, for all delirium people are treated according to the guidelines and they all get haloperidol in Holland. So there is an ethical problem there.