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Chapter 3

Outcomes associated with the nationwide introduction of Rapid Response Systems in the Netherlands

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Abstract

Objective: To describe the effect of implementation of a Rapid Response System (RRS) on the composite endpoint of cardiopulmonary arrest, unplanned ICU admission, or death.

Design: Pragmatic prospective Dutch multicenter before-after trial, Cost and Outcomes analysis of Medical Emergency Teams trial.

Setting: Twelve hospitals participated, each including two surgical and two non-surgical wards between April 2009 and November 2011. The Modified Early Warning Score and Situation-Background-Assessment-Recommendation instruments were implemented over 7 months. The rapid response team was then implemented during the following 17 months. The effects of implementing the rapid response team were measured in the last 5 months of this period.

Patients: All patients 18 years old and older admitted to the study wards were included. **Measurements and main results:** In total, 166,569 patients were included in the study representing 1,031,172 hospital admission days. No differences were observed in patient demographics between periods. The composite endpoint of cardiopulmonary arrest, unplanned ICU admission, or death per 1,000 admissions was significantly reduced in the rapid response team versus the before phase (adjusted odds ratio 0.847; 95% CI, 0.725-0.989; *p*=0.036). Cardiopulmonary arrests and in-hospital mortality were also significantly reduced (odds ratio, 0.607; 95% CI, 0.393-0.937; *p*=0.018 and odds ratio 0.802; 95% CI, 0.644-1.0; *p*=0.05, respectively). Unplanned ICU admissions showed a declining trend (odds ratio 0.878; 95% CI, 0.755-1.021; *p*=0.092), whereas severity of illness at the moment of ICU admission was not different between periods.

Conclusions: In this study, introduction of nationwide implementation of rapid response systems was associated with a decrease in the composite endpoint of cardiopulmonary arrests, unplanned ICU admissions and mortality in patients on general hospital wards. These findings support the implementation of rapid response systems in hospitals to reduce severe adverse events.

Introduction

Patients who experience adverse events during their hospital stay, including cardiopulmonary arrest, unplanned ICU admissions and unexpected death, show clear signs of deterioration in the hours preceding the event. 1,2 Rapid Response Systems (RRSs) have been developed for timely identification and treatment of patients on general wards at risk for clinical deterioration. 3 RRSs are designed as a threecomponent system. 4 The two primary components are the afferent and efferent limbs. The afferent limb comprises the early detection of the deteriorating condition by systematic measurement of vital signs using a track and trigger system. 5-7 When measures reach a certain threshold, the efferent limb is activated and the Medical Emergency Team or Rapid Response Team (RRT) is called and responds to the patient's bedside. These teams are most often composed of ICU physicians together with ICU nurses. 8 The final component is the education, data collection and analysis limb to aid in (sustained) implementation within the institution.

Up to this moment, only two randomized studies have been performed investigating the effectiveness of RRSs. A large randomized trial from Australia, the Medical Early Response Intervention and Therapy (MERIT) study, failed to show an impact of introduction of an RRT on a composite endpoint including death, cardiac arrest and ICUadmission. 9 The second study from the United Kingdom demonstrated a reduction in hospital mortality after introduction of an RRT. ¹⁰ Apart from these studies, many smaller less well-controlled studies have been published generally reporting a decline in cardiac arrest rates following introduction of an RRT. ¹¹

In 2008, implementation of RRS was mandated by the Dutch government. 12 We took the opportunity to study the effects of this nationwide implementation of RRS on outcome of patients admitted to general hospital wards. Primary endpoint was the incidence of the composite endpoint of cardiopulmonary arrest, unplanned ICU admission, or death.

Methods

Trial design

The study protocol has been described previously. 13 In short, the Cost and Outcomes analysis of Medical Emergency Teams (COMET) multicenter study was designed as a prospective, pragmatic before-after multicenter trial enabling the analysis of clinical outcomes after sequential introduction of the RRS components. Twelve of the originally planned 14 Dutch hospitals participated throughout the study. Two hospitals were withdrawn during the study after major local reorganizations with changes in case-mix from surgical to medical patients on COMET-wards. The withdrawal of study centers was performed without knowledge of incidence of study endpoints. Therefore, these two hospitals were excluded from final analysis.

Two large university hospitals (number of beds, 882-1,000), eight large teaching hospitals (number of beds, 359-1,070) and two smaller regional hospitals (number of beds, 290-325) completed the study. Each hospital included four study wards, two surgical and two medical wards. All patients were 18 years or above.

Patients who were readmitted to the hospital were not excluded from the analysis. These patients were considered to be a new hospital admission. The trial design was determined a priori and is shown in Figure 1.

Figure 1. Design of the COMET study.

Following the baseline period of 5 months, the Modified Early Warning Score (MEWS)/Situation-Background-Assessment-Recommendation (SBAR) was implemented for 7 months and subsequently followed up by 17 months in which the rapid response team (RRT) was available. Effects of the RRT on outcomes were measured during the last 5 months and compared with the 5-month baseline period. During the entire length of the study, data were collected on all the endpoints. For further clarification, hospitals were able to start with the study in a 3-month time period. The total study took 30 months, in which each hospital participated for 27 months.

The before period consisted of 5 months in which baseline data was prospectively collected. The implementation of RRS was divided into two phases. Within the first phase (7 months) the MEWS (Modified Early Warning Score) and the SBAR communication tools (Situation-Background-Assessment-Response instrument) were implemented (Appendix A). In the second phase, lasting a total of 17 months, the RRT was introduced. The last 5 months of this phase were used to measure the effects on outcome of patients compared to the before period and will be referred to as "final RRT period". These 5 months comprise the same months of year as the before period.

Outcomes

The primary outcome is the composite endpoint of cardiopulmonary arrest, unplanned ICU admission, or death while being admitted on a COMET ward per 1,000 admitted patients. Intensive care admission did not include medium care or other high

dependency units. Intensive care was defined according to the criteria from the Dutch National Intensive Care Evaluation (NICE) registry. ¹⁴ The composite endpoint was chosen in accordance with previous studies ⁹ because of the low number of patients anticipated to reach the individual components of this endpoint.

Secondary endpoints were the individual components of the composite endpoint and the outcomes per 1,000 admissions days. Cardiopulmonary arrest was defined as an event for which the cardiopulmonary arrest team started cardio pulmonary resuscitation (CPR), using chemical resuscitation and/or manual chest compressions and/or respiratory ventilation (irrespective of type). Unplanned ICU admissions were registered according to the definitions of the Dutch NICE registry as admissions that were unscheduled and could not be delayed for at least 12 hours without risk. All hospitals had followed training in data collection and data definitions as used in the NICE registry.¹⁴

Details of the interventions

Within each participating hospital, all physicians and nurses working on a COMET ward were trained using standardized toolkits, including pocket cards and posters provided by the primary investigators. Specifically, during the MEWS phase, participants were trained in using the MEWS 15 and SBAR communication tool. 16 Determination of the MEWS was mandatory whenever at least one of the measured vital signs was outside its normal range or when considered necessary by the treating physician or nurse. Upon reaching the threshold of three or more points of the MEWS, the responsible physician on that ward was directly notified with communication structured using the SBAR tool. Deviation from the MEWS threshold was allowed in specific circumstances based on patient characteristics for instance in a patient with chronic hypoxemia, but should be clearly mentioned by the physician within the patient chart.

The RRT included both an ICU nurse and a physician who was at least trained in Fundamental Critical Care Support [\(www.fccs.nl\)](http://www.fccs.nl/). Description of activation of RRTs is presented in Figure 2. During the study, no structural changes in data collection charts, medical record keeping or treatment guidelines were introduced.

Sample size

The calculation of the sample size has been described in detail previously. 13 About twice the originally planned number of 27,720 admissions, equally divided over the before and RRT periods, was available for analysis. The actual analysis to detect if the RRT period would show a lower incidence of patients experiencing the composite endpoint or its components by at least 4 (from 10 to 6) per 1,000 admissions, was based on 54,479 admissions, 26,659 stemming from the before period and 27,820 from the final

RRT period. Considering increased numbers of admissions available for analysis, the level of significance was set at a two-sided rather than the originally planned one-sided α of 0.05.

Figure 2. Algorithm for RRT activation.

The algorithm displays the protocol of handling positive MEWS values and all subsequent actions which either nurse or physician has to undertake together with set time limits.

Data acquisition

Admission data of patients who had spent time on a COMET ward at any time during the study observation period were provided by the information departments of participating hospitals. Data on cardiopulmonary arrest, unplanned ICU admission, and death and RRT activations on COMET wards were collected with clinical report forms.

Data presentation and statistical analysis

Incidences of cardiopulmonary arrest, unplanned ICU admission and death, both as composite endpoint and each separately, are presented graphically over time for the before, MEWS, RRT implementation, and final RRT periods respectively. Incidences were calculated per 1,000 admissions. Admissions were counted when a patient had spent at least 1 day of his admission on a COMET ward. Inpatient days were counted when a patient had spent some part of the day on a COMET ward.

Generalized linear mixed modelling (GLMM) was applied to assess differences in outcomes per 1,000 admissions between the before and final RRT periods while correcting for potential confounding following the before-after study design.

Potential confounders were identified following 1) cross-tabulation of categorical variables (sex, emergency admission, hospital) with the before and final RRT periods or *t* testing for the difference in patients' age between the before and final RRT periods and 2) simple univariable logistic regression analyses on the composite outcome with the same variables (sex, emergency admission, hospital, age). Seasonality - reflecting differences in risk of cardiopulmonary arrests, unplanned ICU-admission, or death by calendar month 17,18 – could be ignored, because in each hospital the included months of the year were identical for the before and final RRT periods.

In the GLMM, a binomial distribution was assumed for the composite primary endpoint and for deaths. For unplanned ICU admissions, a binomial distribution was assumed after recoding the original count variable into a dichotomous one, expressing whether patients were at least once admitted to the ICU or not during their stay (no convincing model fit could be achieved under the assumption of Poisson distributed original ICU admission counts). For cardiopulmonary arrests a Poisson distribution was assumed because of its observed (extremely) low incidence. No offset variable was taken into account. Potential confounders were included in GLMM as fixed or random variables. Hospitals were modelled as a random variable, accounting for differences in background incidence (level) and varying impact of the intervention (slope) while simultaneously controlling for the differentially distributed numbers of admissions by hospital during the before and final RRT periods. Age of patients was modelled as a random component, whereas patients' sex and admission type (planned vs unplanned/emergency) were modelled as fixed variables. All analyses were performed in SPSS version 20.0.0.1 (SPSS INC, Chicago, II).

The uncorrected odds ratios (ORs) and ORs after correction for confounding are reported along with their CIs and corresponding *p* values. In deviation from the published study protocol 13, the decision was made to simplify the analyses. We first nested admissions within hospitals rather than within the ward types as clusters because during the introduction, implementation, and maintenance of the RRSs at the local level, hospitals seemed more distinct than ward types. Secondly, it was decided to compare the before and final RRT periods as whole periods and to refrain from the analysis of data by successive months, because the latter approach introduced complex dependencies over time, in case admissions included two or more months.

Ethics approval

The medical ethics committee of the Academic Medical Center in Amsterdam waived the need for formal evaluation of the study due to the obligatory nature of the intervention and the observational nature of the study. Consequently, the need for informed consent was not applicable. The trial was registered at the Dutch Trial Register [\(www.trialregister.nl\)](http://www.trialregister.nl/) under number NTR2706. All authors hereby declare that all experiments have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki, updated October 2008.

Funding for the primary investigators of the study was provided by the Academic Medical Center and Leiden University Medical Center. Each participating hospital provided staff for training of their personal personnel and acquisition of study data.

Results

Characteristics of the study population from the 12 hospitals are presented in Table 1. Patients could be transferred during their hospital admission between non-COMET wards to COMET wards and vice versa. Therefore, the ratio of COMET admission days to the total length of hospital admissions was calculated, ranging from 0.97 to 0.98 in the different study periods.

Table 1. Characteristics of study population

RRT = Rapid Response Team, COMET = Cost and Outcomes analysis of Medical Emergency Teams.

^a Based on 26,659 admissions, excluding one hospital without provided information on emergency.

^b Based on 37,883 admissions, excluding one hospital without provided information on emergency.

Figure 3 shows the primary outcome, that is, the number of patients per 1,000 admissions with a cardiopulmonary arrest, unplanned admission to the ICU, or death while being admitted to a COMET ward. The number of patients who reached the primary outcome decreased from 37.14 (95% CI, 34.94 – 39.34) per 1,000 admissions in the before period to 32.92 (95% CI, 30.88 – 34.95) in the final RRT period (Figure 3). The unadjusted OR of reaching the primary endpoint was 0.88 for the last 5 months of the RRT phase relative to the before phase. The number of patients reaching the primary endpoint in the MEWS and the RRT implementation period (Figure 3) were 39.14 (95% CI, 37.24 – 41.03) and 37.28 (95% CI, 35.86 – 38.70) respectively. Per 1,000 COMET inpatient days, the composite endpoint was reached 5.90, 6.13, 5.98, and 5.77 times in the before, MEWS, RRT implementation phase, and final RRT periods respectively.

Figure 3. Composite endpoint per 1,000 admissions. The primary endpoint, that is, the number of patients per 1,000 admissions with a cardiopulmonary arrest, unplanned admission to the ICU, or death while being admitted to a COMET ward, is shown. The incidence of the composite endpoint is shown including its 95% CI. MEWS = Modified Early Warning Score, RRT = rapid response team.

The results for the individual components of the primary outcome presented per 1,000 admissions are given in Table 2. The number of cardiopulmonary arrests remained stable in the before and MEWS periods and gradually declined in the RRT implementation and final RRT periods. The number of unplanned ICU admissions was similar in the before, MEWS and RRT implementation periods, but dropped in the final RRT period. Mortality increased from the before to the MEWS period and fell back again to the baseline level in the RRT implementation period, before it further decreased in the final RRT period.

Table 2. Secondary outcomes per 1,000 admissions

RRT = Rapid Response Team.

^a Including multiple unplanned ICU admissions per patient.

Interestingly, the composite endpoint was almost entirely composed of unplanned ICU admissions and deaths; cardiopulmonary arrest was a less frequent event. Per 1,000 COMET inpatient days, the point estimates for the before, MEWS, RRT implementation and final RRT periods are 0.31, 0.30, 0.25, and 0.21 for cardiopulmonary arrests, 3.15, 3.06, 3.12, and 2.99 for unplanned ICU admissions, and 3.23, 3.52, 3.29, and 3.09 for deaths respectively.

Table 3 shows the ORs for the primary and secondary endpoints. The unadjusted ORs of having a cardiopulmonary arrest in the final RRT period relative to the before period was 0.626 (95% CI, 0.41-0.95), of being admitted unexpectedly at least once to the ICU 0.881 (95% CI, 0.77–0.99) and of dying 0.865 (95% CI, 0.76–0.97). Adjustment for casemix variables was performed for potential confounders gender, age, individual hospital, and urgency of admissions, while simultaneously accounting for clustering of admissions within hospitals. Preparatory analyses revealed associations of these variables with the composite endpoint, whereas sex, hospital and emergence level were also differentially distributed over the before and after periods (data not shown). The benefits of the RRT turned out slightly better after correcting for confounding variables while taking into account clustering of admissions within hospitals.

Table 3. Odds ratios of composite endpoint and its individual components for the Rapid Response Team final period versus the before period, corrected for sex, age, hospital and emergency of admission.

OR = odds ratio.

aA generalized linear model (GLM) model based on Poisson-distributed cardiopulmonary arrest with identity link converged during its iteration and showed a *p* value of 0.018; the corrected odds ratio reported stems from a nonconverging Poisson-based GLM model with a log link which is slightly more conservative (*p*=0.024).

b Odds ratio presented for being unexpectedly admitted at least once to the ICU.

Number of admissions in before period = 26,659; number of admissions in rapid response team period = 27,820.

Appendix B shows the characteristics of patients reaching the individual components of the primary endpoint for all study phases. Statistical comparisons were restricted to the before and RRT periods of the study only. During the before period, more patients were transferred to the coronary care unit and less patients to other hospitals or other destinations after a cardiopulmonary arrest (*p*=0.013) when compared to the RRT period. Patients who died were younger in the RRT phase (75.0; SD, 14) compared with the before phase (76.8; SD 12) (*p*=0.021).

Only in the RRT implementation and final RRT phases, the RRT was available for the care providers. The call rate in the RRT implementation phase was 6.8/1,000 admitted patients and increased to 7.3/1,000, see Appendix C. In this study, the RRT was primarily called by the responsible physician. However, in the RRT implementation phase, 15% of the RRT calls were initiated by a nurse which decreased to 9% in the RRT phase with a seemingly corresponding increase of activations by the resident. Rarely, do not attempt resuscitation (DNAR) orders were instituted after an RRT was called.

Discussion

The COMET study is the largest trial which has been performed investigating the effectiveness of RRSs. 9 Eventually, 12 Dutch hospitals participated in this trial in which an approximately 15% adjusted risk reduction in severe adverse events, including cardiac arrests, unplanned ICU admissions and in-hospital mortality, was found.

Regarding the individual components of the primary endpoint, full implementation of the RRS resulted in lower rates of death and cardiac arrest and only a trend for unplanned ICU admissions. It has been argued that effective RRS may lower the rate of ICU admission by earlier detection and treatment of deteriorating patients but also may increase ICU admission if deteriorating patients are transferred to the ICU for treatment. Therefore, ICU admission rates may underestimate the beneficial effect of RRSs.

As recently reviewed, 42 studies have been published describing the effectiveness of RRSs. ¹⁹ Many of these studies were relatively small and underpowered to find effects on clinically relevant endpoints. Methodological quality was suboptimal in most studies. ¹⁹ In some studies, a reduction in the incidence of cardiac arrests was reported. 20-23 However, interpretation of this reduction is difficult as no adjustment was made for DNAR policies. It cannot be ruled out that institution of RRTs lead to an increase of DNAR orders and consequently to less registered CPR attempts. 24,25

Two large, randomized, well-designed studies have been published on the effects of RRSs on outcome of in-hospital patients. The first study by Priestley et al 10 used a stepped wedge design and was performed in United Kingdom and included 7,450 patients. Introduction of a RRT lowered in-hospital mortality, with an odds ratio of 0.52.

By contrast, the MERIT trial randomizing 23 Australian hospitals to introduce RRS or to continue usual care did not show an improvement on a composite endpoint consisting of unexpected death, unplanned ICU admission or cardiac arrest after introduction of an RRS. ⁹ Several possible explanations for these negative results have been suggested, including contamination of the control group and secondly, lack of power in this cluster randomized design. Maybe more importantly, the time taken for implementation of RRSs may have been too short for optimal functioning. 26-30

Interestingly, a marked difference was present in the proportion of patients reaching the endpoints. In the Australian MERIT study, at baseline, almost 5 per 1,000 admitted patients were transferred unplanned to the ICU, in the COMET study, 20 per 1,000 were admitted to the ICU. Most likely explanation for this difference is the fact that in the COMET study only patients that were admitted to four selected surgical and medical wards per hospital were included, whereas all hospital patients were included in the MERIT trial. Alternatively, we cannot exclude that differences in ICU admission policies or availability of ICU beds may account for the different ICU admission rates. Death rates were also considerably lower in the MERIT study, but this can be explained by the fact that only unexpected deaths were included in the MERIT study in contrast to all deaths in the present study. It may well be that the effects of RRSs depend on the severity of illness and other characteristics of the population it is introduced to.

In 2007, the Dutch government demanded that RRSs should be instituted in all hospitals in the Netherlands. Due to this mandatory nature of RRS in the Netherlands, any form of a randomized trial, including a stepped wedge design, was not feasible. Therefore, the COMET study was designed with a prospective before-after methodology, with the inherent risk that associations between intervention and outcome may not be causal. 31 For instance, severity of illness may have changed over time, potentially influencing the rates of mortality, cardiac arrest or ICU admission. Although baseline characteristics were very similar in the different study periods, we cannot fully rule out this possibility. Also, simultaneous interventions - which may include the SURgical Patient Safety System checklist in surgical patients ³² - or general background trends during the study could also influence our findings. Consequently, caution should be taken in this respect when interpreting the study results.

In our study, a slightly increased death rate was shown in the phase in which the MEWS data were collected but without institution of a RRT. No clear explanation can be given for this finding. It could be related to seasonal effects. In this respect, it should be emphasized that the primary comparison between baseline and full implementation of the RRS is not influenced by seasonal factors because both periods comprised the same months of year in all participating hospitals. Several arguments do support a causal interpretation of the association between the RRS and the studied severe adverse

events. First, the working mechanism of RRSs makes a positive impact on incidences of severe adverse events plausible, and proactive monitoring of patients is very likely to be beneficial. 33 Second, we improved the internal validity of our before-after design by adjusting for potential confounders including gender, age, individual hospital and urgency of admissions. The strength of the association of the RRS with the composite endpoint increased with ORs being 0.85 (95% CI, 0.72-0.99) and 0.88 (95% CI, 0.77 – 0.99) with and without adjustment for confounders respectively. Third, during the study and also in 11 of the 12 hospitals (data not shown), the effect of sequential introduction of the RRS resulted in a consistent and gradual decline of the proportion of patients reaching the endpoints over time.

Interestingly, our study was the first to perform the analysis of sequential introduction of the components of an RRS. Our data may suggest that instituting only the afferent limb of the RRS, which is the MEWS/SBAR, may not be as effective in decreasing the number of cardiac arrests, unplanned ICU admissions, or deaths. This suggestion should only be interpreted as hypothesis formulation also because these findings were not corrected for seasonal influences. It is very likely that increased utilization of the system and its components is likely to result in improved clinical outcome during the entire study period. ³⁴

The results of the COMET study support the continuing efforts regarding implementation of RRS and optimization of current systems. A more mandatory nature of implementation and measurement of outcomes would assist in the continual optimization and research into RRS.

Based on the results of this study, introduction of an RRS with the MEWS and SBAR for early identification and a RRT for early management of patients at risk for deterioration was associated with a decrease in the incidence of severe adverse events including death, unplanned ICU admission and cardiac arrest. As part of the COMET study, a budget impact analysis will be performed in further analyses.

Authors contributions and Acknowledgements

JL and ABR are both primary authors and share responsibility for the logistical process together with data entry, validation and analysis. Principle design of the study was performed by JL, EdJ and MD. Data analysis was performed primarily by MD and writing of the manuscript by JL and ABR with supervision of EdJ and MD. All co-authors read and acknowledge the content of this manuscript.

JL and ABR had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Appendix A. Modified Early Warning Score and Situation-Background-Assessment-Recommendation communication tool

Modified Early Warning Score (MEWS)

Worried about patient's condition: 1 point

Urine production below 75 milliliter during previous 4 hours: 1 point

Saturation below 90% despite adequate oxygen therapy: 3 points

Upon reaching 3 or more points \rightarrow call resident in charge

The MEWS score was implemented as the tool for ward staff to identify the patient at risk of deterioration. The described method was adapted from Subbe et al. ¹⁵

The SBAR communication instrument.

Unless stated otherwise, numbers represent percentages. Statistical comparisons were performed between the before and RRT phase. The Chi-square test, Fisher's exact test, T-tests were performed as appropriate.

 $CPR =$ cardiopulmonary resuscitation; $SD =$ standard deviation; $IQR =$ interquartile range; $SAPS =$ simplified acute physiology score; APACHE = acute physiology and chronic health evaluation.

Appendix C. Rapid Response Team call rate and interventions

This table represents the activation of RRTs. Due to unreliable administration of the consultations by the RRTs; these numbers are an underestimation of the real time RRT activations. Unless stated otherwise, numbers represent percentages. The category 'other' includes direct outcome after RRT consultation. This includes Medium Care or High Care transfer, transfer to other nursing ward and miscellaneous.