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Systematic review of telemonitoring in COPD: an update

Abstract

Telemedicine may support individual care plans in people with chronic obstructive pulmonary disease (COPD), potentially improving the clinical outcomes. To-date there is no clear evidence of benefit of telemedicine in this patients. The aim of this study is to provide an update on the effectiveness of telemedicine in reducing adverse clinical outcomes.

We searched the Pubmed database for articles published between January 2005 and December 2014. We included only randomized controlled trials exclusively focused on patients with COPD and with a telemedicine intervention arm. Evaluated outcomes were number of exacerbations, ER visits, COPD hospitalizations, length of stay and death. We eventually included 12 randomized controlled trials. Most of them had a small sample size and was of poor quality, with a wide heterogeneity in the parameters and technologies used. Most studies reported a positive effect of telemonitoring on hospitalization for any cause, with risk reductions between 10% and 63%; however only three studies reached statistical significance. The same trend was observed for COPD-related hospital admission and ER visits. No significative effects of telemedicine was evidenced in reducing length of hospital stay, improving quality of life and reducing deaths.

In conclusion, our study confirms that the available evidence on the effectiveness of telemedicine in COPD does not allow to draw definite conclusions; most evidence suggests a positive effect of telemonitoring on hospital admissions and ER visits. More trials with adequate sample size and with adequate consideration of background clinical services are needed to definitively establish its effectiveness.

Key words: Pulmonary Disease, Chronic Obstructive; Telemedicine; Systematic Review; Randomized Controlled Trials as Topic; Home Care Services

Pneumonol Alergol Pol 2015; 83: 476–484

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the most prevalent disease worldwide. The clinical course is characterized by progressive decline in health status, punctuated by acute respiratory exacerbations [1]. These exacerbations have a negative impact on patient prognosis, with progressive disability and increased health care resource use [2,3].

In COPD patients with a previous or recent history of exacerbations, current guidelines recommend education and case management in order to prevent severe acute exacerbations and to reduce COPD-related hospitalizations [4]. Furthermore, strategies aimed to identify and manage exacerbations at early stages are also needed in order to prevent hospitalizations, improve quality of life and to reduce health care cost [5].

Recently, due to an increased accessibility to and lower costs of information and communication technologies (ICT), telehealth applied to both acute and chronic disease has received great attention from the scientific community. Telehealth is defined "the provision of personalized health care from a distance". Other terms are used in this field; in particular "telemedicine" is often reserved for clinical and patient care applications [6]. The ultimate goal of telemedicine is to improve clinical management and quality of life of patients with chronic disease with consequent reduction of health costs [7].

In the latest years, a wide array of telemedicine applications have been developed, using

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DOI: 10.5603/PiAP.2015.0077
Received: 31.07.2015

ISSN 0867–7077

different devices (telephone, computer, or wearable and not wearable devices) . These applications are able to collect several parameters such as peripheral oxygen saturation, body weight, temperature by means of dedicated devices able to directly transmit data, or commercial measuring devices (e.g., pulse-oxymeter) that are connected to a transmitting device (e.g., a cellular telephone) that acts as a "gateway" to transmit the data. In some instances, the readings are obtained using a commercial device and the information is manually transmitted by the patients, for example by punching it on a keyboard connected to a transmitting device. Data transmission can be synchronous or asynchronous with data collection. The information transmitted by the telemonitoring systems are usually evaluated by healthcare professionals, such as doctors or nurses. In case of abnormal readings or when scheduled measurements were missing, a pre-specified protocol is put in action to respond to the situation. In some cases, telemonitoring systems can generate alerts to warn the personnel when readings are outside a specified range of normality.

In theory, telemedicine may help to better assist patients with physical limitations, and those who need frequent evaluation of their health status. Furthermore, in conditions characterized by exacerbations, such as COPD, it may help to detect these events earlier, with more timely treatment and reduction of risk of adverse clinical outcome. Telemedicine may also foster greater patient self-management and less costly interventions [8]. Many trials have been performed to assess the effectiveness of telemonitoring in COPD patients to reduce health care resources consumption and health care costs, and to improve quality of life. The results of these studies, however, have been conflicting, and to-date, there is no clear evidence benefit of telemonitoring in COPD.

The aim of this study is to provide an update on the available data published in the last 10 years on the effectiveness of telemedicine in COPD in reducing emergency room (ER) visits, hospitalizations and deaths and in improving quality of life.

Methods

This systematic review is performed according with PRISMA guidelines. We searched the Pubmed database for articles published between January 2005 and December 2014. The MeSH keywords used were "telemedicine" and "COPD". Titles and abstracts of studies matching our search strategy were screened and the potentially eligible ones were obtained in full text for evaluation. The bibliography of selected studies were also searched to retrieve additional articles.

In order to reduce heterogeneity, we limited our review to randomized controlled trials exclusively focused on patients with COPD and with a telemedicine intervention arm, defined as delivery of health services via remote telecommunications. Studies including only telerehabilitation or self-management or teleconsultation were excluded. Articles published in languages different than English were also excluded.

The outcomes we took into account were number of exacerbations, ER visits , COPD hospitalizations, length of stay, and death. We also looked at quality of life and patients' satisfaction.

Results

Literature search and studies general characteristics

The literature search identified 182 potentially relevant papers. After reviewing the titles and abstracts, 50 were selected for a closer examination. 38 articles were excluded because they did not satisfy inclusion criteria. Twelve randomized controlled trials were eventually included in our review (Figure 1). A summary of the key characteristic of all 12 trials is shown in Table 1. Most studies were performed in Spain (5 papers). Almost all trials were monocentric.

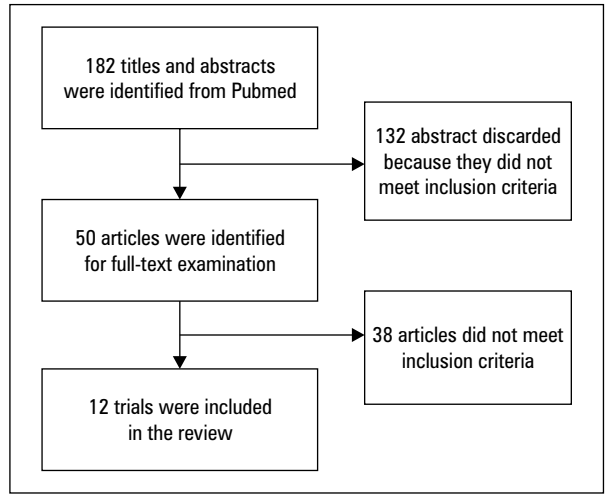

Figure 1. Study flow diagram

Table 1. Characteristics of included studies

Study	Country	N	Mean age (sd) Control / intervention	COPD stage	Technology	Measured parameters	Type of intervention
Casas 2006 [10]	Spain -Belgium	155	72 (9)/ 70 (9)	All	Telephone (Web -based call center)	None	Comprehensive patient assessment with weekly phone calls during first month to reinforce self-management Accessibility to a specialized nurse case manager through a web-based call center who could access to patients records; if necessary, planning non-scheduled home visits
de Toledo 2006 [20]	Spain	157	72 (8)/ 71 (8)	All	Support for video-conference Computer with Internet connection	Health questionnaire Spirometry	Patients could contact the call center for technical or health problems. In case of health problems 10 questions were asked to assess illness severity Regular nurse home visits, with access to on-line patient's clinical informations and doing a spirometry
Garcia--Aymerich 2007 [11]	Spain	113	73 (9)/ 72 (10)	All	Telephone (Web -based call center)	None	Comprehensive patient assessment with weekly phone calls during first month to reinforce self-management Specialized nurse case manager available through a web-based call center who could access to patients records; if necessary, planning of non-scheduled home visits
Koff 2009 [17]	USA	40	65(8.2)/ 66.6 (9.1)	GOLD stage 3–4	Technology platform used to enter and transmit results using home telephone line	Symptoms-based questions FEV_1 6-min walking test Oxygen saturation	Daily data collection; patients could call in case of problems Data checked by a respiratory therapist In case of alert therapist called the primary care physician
Lewis 2010 [14]	United Kingdom	40	73/ 70	Moderate-severe COPD	Handheld telemonitor connected with medical devices; data transmission via internet connection	Questions about chest over the preceding day or night Temperature Oxygen saturation	Data recorded twice a day, transmitted to a website accessible to the Team Automatic email message to Team in case of alerts, with subsequent call to the patient or message issued through the monitor's screen
Antoniades 2012 [18]	Australia	44	68 (9)/70 (10)	Moderate-severe COPD	Laptop computer with digitally integrated health devices with internet connection	Spirometry Weight Temperature Blood pressure Oxygen saturation Electrocardiogram Sputum color and volume Symptoms Medication usage	Daily parameters measurement, with possibility to record symptoms and change of medication , reviewed by a nurse In case of a clinical alert the nurse could call the patient or local doctor
Chau 2012 [13]	China	40	72.22 (6.13)/73.5 (6.05)	Moderate-severe COPD	Mobile phone connected with medical devices	Oxygen saturation Heart rate Respiratory rate	First nurse home visit for all groups participants with self-care education Patients collected clinical data three times a day, sent to on-line platform, monitored by a nurse

Table 1 cd. Characteristics of included studies

De San Miguel 2013 [15]	Australia	80	74/ 71	COPD with domiciliary oxygen	HealthHub (portable unit with display) connected to telephone line	Blood pressure Weight Temperature Heart rate Oxygen saturation Question related to general state of health	Daily parameter measurement, automatically transmitted via telephone to a secure Web site, daily monitored by a nurse Generation of alert in case of parameter alteration or missing data: the nurse contacted the participants over the telephone and recommend a GP visit if necessary
Jòdar--Sànchez 2013 [21]	Spain	45	71 (10)/ 74 (8)	COPD with chronic respiratory failure in LTO	Medical devices connected to the patient's home telephone line	Every day: Oxygen saturation (daily) Heart rate (daily) Blood pressure (daily) Spirometry (2/week)	Daily data collection, sent to the Call Centre In case of alert call center contacted patient; if confirmed, generation of therapeutic strategy
Pedone 2013 [12]	Italy	99	75.4 (6.7)/ 74.1 (6.4)	GOLD stage II-III	Mobile phone connected via bluetooth to a pulse-oxymeter and a wristband that contained sensors for clinical parameter measurement; data transmission via telephone	Oxygen saturation Heart rate Near-body temperature Overall physical activity	Data measured every three hours during the day, evaluated daily by a physician skilled in respiratory care; Alert generation in case of parameter alteration: physician contacted telephonically patients for check and therapeutic strategy
Pinnock 2013 [16]	United Kingdom	256	68.4 (8.4)/ 69.4 (8.8)	All	Touch screen telemonitoring equipment connected to the patient's home telephone line	Daily questionnaire about symptoms and treatment use Oxygen saturation	Daily data recording, monitored by the supporting clinical team In case of clinical alerts , the team contacted the patient by telephone to undertake clinical assessment for patient management
Segrelles Calvo 2014 [19]	Spain	60	72.7 (9.3)/ 75 (9.7)	Severe o very severe COPD with long-term home oxygen therapy	Medical devices with automatic data transmission via a modem through patient's telephone line	Blood pressure (daily) Oxygen saturation (daily) Heart rate (daily) Peak expiratory flow (3/week)	Daily parameters measurement, transmitted to a Clinical Monitoring Center In case of alert, a nurse contacted the patient and eventually escalated to Pneumologist for management.

Abbreviations: COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in the 1st second; GP: general practitioner; LTO: long-term oxygen therapy

Trials were published in 8 different journals; 8 studies were published in Journal of Telemedicine and Telecare, Telemedicine and e-HEALTH, Respiratory Medicine and European Respiratory Journal (2 studies each). Inclusion criteria were very heterogeneous, the GOLD stages selected differed across studies, and a recent history of hospitalization for COPD-exacerbation was not required by all trials. Exclusion criteria were heterogeneous as well, but most studies excluded patients with cognitive impairment or in palliative care.

In general, the sample size of the studies was small (5 trials have less than 50 participants). Mean age range varied from 65 to 73 years. The follow-up period ranged from 20 days to 1 year. Five trials included only moderate-severe or severe COPD. Educational intervention were utilized in 5 studies, in 3 studies it was offered to both arms, in the others only to the intervention group. The outcomes most frequently studied were hospital readmissions, ER visits, patient satisfaction, and quality of life.

The quality of the studies evaluated according to the Cochrane Guidelines [9] was at best fair. As it was expected in studies on this topic, no study used masking of the treatment allocation. Blinded outcome assessment and statistical analy-

Table 2. Risk of bias in the included studies.

First author	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
Casas 2006 [10]	L	L	Not blinded	U	L	L	H
de Toledo 2006 [20]	U	U	U	U	U	L	L
Garcia-Aymerich 2007 [11]	L	L	Not blinded	U	H	H	L
Koff 2009 [17]	H	U	Not blinded	Not blinded	L	L	L
Lewis 2010 [14]	L	L	U	U	U	L	L
Antoniades 2012 [18]	L	L	U	U	L	L	L
Chau 2012 [13]	H	U	Not blinded	Not blinded	L	L	H
De San Miguel 2013 [15]	L	L	Not blinded	Not blinded	H	H	L
Jòdar-Sànchez 2013 [21]	U	U	U	U	H	L	L
Pedone 2013 [12]	U	U	Not blinded	Not blinded	L	L	L
Pinnock 2013 [16]	L	L	U	L	L	L	L
Segrelles Calvo 2014 [19]	H	U	Not blinded	Not blinded	L	H	L

Criteria defined for quality assessment are based on the Cochrane guidelines [9].
Abbreviations: H, high risk of bias; L, low risk of bias; U, unclear or unrevealed risk of bias.

sis was not used by all studies, and in some cases it was not possible to ascertain whether blinding assessment was used or not. Furthermore, in some studies the outcome data were selectively reported (Table 2).

Telemonitoring characteristics

There was a noticeable heterogeneity in the technologies used. In some cases [10,11], information was obtained by a nurse using questionnaires in telephone interviews, in others [12,13] a mobile phone were used to transmit data collected using commercially available devices. In some instances, a portable unit including measuring devices acted as measuring and transmitting device [14–16]. Data were transmitted using the Internet in eight trials, the broadband mobile phone connection in two trials; while two trials used telephone interviews.

In all studies a health care professional (e.g. nurse) monitored the collected data. The data collected and the action taken in response to abnormal readings varied across studies. The data collected ranged from health questionnaires only to multiparametric data collection, including spirometry or peak expiratory flow. The parameters most frequently used for telemonitoring were peripheral oxygen saturation (9 trials), health status questionnaires (6 trials) and heart rate (5 trials). The action taken could be follow-up telephone calls, calls by a nurse with access to patients' personal records [10,11], home visits, or scheduling of ambulatory visits or hospital admission, depending on the severity of abnormalities in monitored parameters. In most instances, the telemonitoring systems were equipped with algorithms that could generate an alert in case of change in measured parameters or in case of loss of data measurement for one or more days.

Effect on hospital admissions

This outcome was evaluated in 8/12 included studies (Table 3), with results not completely comparable because of differences in the asso-

Table 3. Studies outcomes: differences between telemedicine vs control group

First author	All causes readmissions	COPD-related readmissions	Length of stay	ER visits	Deaths	QoL	Satisfaction
Casas 2006 [10]	Improved*	–	–	–	Worsened	–	–
de Toledo 2006 [20]	Improved*	–	–	Improved	Worsened	–	–
Garcia-Aymerich 2007 [11]	–	Improved*	–	–	–	Not modified	–
Koff 2009 [17]	–	Improved	–	Improved	–	Improved*	Improved
Lewis 2010 [14]	–	–	–	–	–	Not modified	Improved
Antoniades 2012 [18]	Improved	Improved	Not modified	–	–	Improved	–
Chau 2012 [13]	–	Worsened	Worsened	Worsened	–	Not modified	Improved
De San Miguel 2013 [15]	Improved	Improved	Improved	Improved	–	–	Improved
Jòdar-Sànchez 013 [21]	Worsened	–	Worsened	Improved	–	Improved	Improved
Pedone 2013 [12]	Improved	–	–	–	–	–	–
Pinnock 2013 [16]	Not modified	Improved	Improved	–	Improved	Not modified	–
Segrelles Calvo 2014 [19]	Improved*	–	Improved*	Improved*	Improved	–	Improved

ER: emergency room; QoL: quality of life; *: statistically significant.

ciation measures used. Two studies [13,17] only reported data on COPD-related admission. Most studies (6/10) reported a positive effect of telemonitoring on hospitalization for any cause, with risk reductions between 10% [18] and 40% [15], with the noticeable exception of Segrelles et al. that reported a risk reduction of 63% [19]. In only three of these positive studies [10,19,20], however, the results reached statistical significance. One study [21] reported an increase in hospitalizations in the telemonitored group, with an average number of hospitalizations per patients in the follow-up period (4 months) of 0.38 in the telemonitoring group and 0.14 in the control group.

Effect on COPD-related hospital admissions

Half of the included studies evaluated this outcome (Table 3). Most of them (4/6) reported a reduction in number of COPD-related hospitalizations, with a risk reduction ranging from 14% [18] to 69% [17]; no study, however, reached statistical significance. Only Chau et al. [13] reported a non-statistically significant increase in number of COPD-related hospitalization; Pinnock et al. did not document a difference between the two groups [16].

Effect on hospital length of stay

This outcome was evaluated in 7 studies (Table 3). Four studies [12,13,16,21] documented an increase in length of stay in telemedicine group, with mean differences ranging from +1.5 to +3 days. On the contrary, a reduction in length of stay was reported in two studies[15,19], of 5 and 9 days, respectively. However, only the study by Segrelles et al. reached statistical significance. Antoniades et al. found no difference in length of stay of the two groups.

Effect on emergency room visits

This outcome was evaluated in 6 of 12 trials included in our review (Table 3). With the exception of Chau et al., that found an 87% increase in the risk of ER visits, all the other studies reported a reduction in risk ranging from 17% [15] to 55% [19]. However, with the exception of Segrelles et al., none of these studies reached statistical significance.

Effect on mortality

Four studies evaluated this outcome, reporting very discordant results (Table 3): Casas et al. and De Toledo et a. documented an increase of risk of death in telemonitor group of about 18%; Pinnock et al. [16] and Segrelles et al. [19] reported a risk reduction of 25 and 45%, respectively. None of these results was statistically significant.

Effect on quality of life

This outcome was evaluated in 7 studies (Table 3). Data were not well comparable because of

different quality of life questionnaires were used. Five studies used the St. George's Respiratory Questionnaire (SGRQ). A statistically and clinically (>= 4 points) significant improvement in SGRQ score was reported only by Koff et al. Two trials documented a non-statistically significant change >= 4 points in SGRQ in telemonitoring group compared with control group [18, 21] and four studies did not show differences in quality of life between groups [11,13,14,16].

Other outcomes

Patients' satisfaction was good in all of the 6 trials that reported it. A non-statistically reduction in health care associated costs was reported in the 2 trials that evaluated this outcome.

Discussion

Our study confirms that the available evidence on the effectiveness of telemedicine in COPD does not allow to draw definite conclusions, as the studies on this topic are generally small and of overall poor quality, with many studies not providing all the data needed for a correct and critical interpretation of the results. In line with previous reviews and meta-analysis [22–24], we found that most evidence suggests a positive effect of telemonitoring on the outcomes taken into account, in particular with respect to hospital admissions and ER visits, although statistical significance was reached only by few studies. Only Chau et al. reported a non statistically significant increase of risk in all the outcomes studied (hospitalizations, length of stay, ER visits).

The literature review highlights the importance of baseline treatment offered to the patients. In particular, it can be noticed that the benefit of telemedicine interventions were at best small in studies including education on self-care [13,16] or the patients were already followed in the center in which the experiment took place [14]. Interestingly, when education on self-care was offered only to telemedicine group, the reduction of hospitalizations in the intervention group was more evident [10,11]. Therefore, it is possible that part of the differences in outcomes evaluated by the trials may be explained by clinical services (education on self-management of exacerbations, scheduled follow-up by a physician who knows patients history, etc.) that may offered, either explicitly or implicitly, in a different quantity to patients in the treatment group. This hypothesis seems to be confirmed by the study by Pinnock et al., in which there was a careful optimization of underlying clinical services offered to both groups and in which telemedicine intervention had no effect. The authors concluded that baseline clinical services, rather than telemedicine per se, may be the primary determinants of improved outcomes. Nonetheless, some advantages of telemedicine are identifiable: although not statistically significant, a trend in improvement in all outcomes is evident in almost all studies, regardless of the sample size. Therefore, it is important to gather more information coming from trials of adequate size in which the role of telemedicine *per se* can be separated by the role of clinical services associated with it.

In line with previous reviews and meta-analysis, we did not observe any effect of telemedicine on mortality. These disappointing results only in part unexpected, as even the most promising pharmacological therapies have no clear effect on this outcome in COPD. For example, long-acting beta2-agonists (LABA) or anticholinergic (LAMA) therapy did not significantly reduce mortality or serious adverse events [25,26]. On the other hand, rehabilitation appears to improve dispnoea, quality of life, number of exacerbations, subsequent hospitalizations [27,28] and mortality [29,30]. In this perspective, programs of telerehabilitation may be more effective compared to telemedicine. Few data are available on this topic, but some trials are going on, showing its safety, feasibility [31] and improvement in dispnoea, quality of life and physical activity [32,33].

Despite the reported high patients satisfaction rate, quality of life does not appear to be significantly improved by telemedicine interventions, with the only exception of Koff et al. The most likely explanation to this finding is that the scales used were disease-specific and may not have captured improvement in the overall quality of life.

The overall state of the art of telemedicine in COPD shows that the evidence is still sparse, with studies that can hardly be compared because of different populations (from COPD of any severity to severe COPD in long term oxygen therapy, enrolled in different settings), exacerbation rate before enrollment, wide range of follow up periods (from 2 months to 1 year) and different types of technology used (from telephone interview to multi-parametric monitoring). Furthermore, the heterogeneity of measured parameters makes it impossible to establish which is parameter, or set of parameters, that is most effective for a timely detection of exacerbations. Finally, the background primary care setting is different across studies, and this is a further issue complicating the data comparison.

In addition, it is to underline that the most part of trials excluded patients with cognitive impairment and patients in palliative care; these patients represent a relevant part of population, that can have many benefits from telemedicine, and that consequently should be included in trials, also in order to test the efficacy of telemedicine in a sample of the real population.

As for any review, the search strategy and selection criteria may have introduced bias. At difference with most previous reviews, we only included randomized clinical trials, with exclusion of nonrandomized trials that are known to more frequently lead to positive results. This notwithstanding, our conclusions are in line with most published reviews. Furthermore, we did not take into account trials on telemedicine also including non-COPD patients. This led to the exclusion of some trials, as the one by Vitacca et al [34], that reported a reduction in hospitalizations, ER visits, urgent General Practitioner (GP) calls and exacerbations in the subgroup of COPD patients. Thus, the exclusion of this trial may have led to underestimate the positive effect of telemedicine in our review. However, no different conclusions about the effectiveness of telemedicine were reached by reviews, such as the cited Cochrane review, that included this study.

Conclusions

The role of telemedicine in the management of COPD is still to be elucidated. More trials with adequate sample size and with adequate consideration of background clinical services are needed to establish its effectiveness. These trials should also be designed so that it will be possible to answer some critical questions: what is the population most likely to benefit from the intervention, what is the best set of parameters to collect in order to prevent adverse outcomes, and what the characteristics of a telemedical system should be in order to maximize the adherence of patients that are frequently elderly and with physical and possibly cognitive limitations.

Conflict of interest

The authors declare no conflict of interest.

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