Estimation of Cough Peak Flow Using Cough Sounds

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Abstract: Cough peak flow （CPF）is a measurement to evaluate the risk of cough dysfunction and can be measured using various devices, such as spirometers. However, complex device setup and the face mask required to be firmly attached to the mouth impose burdens on both patients and their caregivers. Therefore, this study develops a novel cough strength evaluation method using cough sounds. This paper presents an exponential model to estimate CPF from the cough peak sound pressure level (CPSL). We investigated the relationship between cough sounds and cough flows and the effects of a measurement condition of cough sound, microphone type, and participant's height and gender on CPF estimation accuracy. The results confirmed that the proposed model estimated CPF with a high accuracy. The absolute error between CPFs and estimated CPFs were significantly lower when the microphone distance from the participant's mouth was within 30 cm than when the distance exceeded 30 cm. Analysis of the model parameters showed that the estimation accuracy was not affected by participant's height or gender. These results indicate that the proposed model has the potential to improve the feasibility of measuring and assessing CPF.

Keywords: Cough sound; Cough peak flow; Microphone; cough ability; cough strength; Bone conduction microphone; smartphone

1. Introduction

Cough peak flow (CPF) is a measurement commonly used to evaluate the cough strength, which reflects the ability to expel airway secretions [1-7], and can predict the extubation [7,8] and reintubation outcomes [9-11]. Values of CPF below 160 L/min have been associated with infective airway clearance [6,7,12], and patients who can generate a CPF of more than 270 L/min have little risk of developing respiratory failure during upper respiratory tract infections [13]. In the previous studies, CPF was measured with various devices, such as flow meters, spirometers, and pneumotachographs. However, not all medical facilities provide these devices [14]. Moreover, the complex device setup, including firmly attaching the facemasks and infection control filters on the patient [1], imposes burdens on both patients and their caregivers. In addition, the measured CPF value can vary depending on the type of facemask and filter.

Therefore, we propose a novel simple evaluation system for evaluating cough ability using cough sounds without the use of the facemask or the filter. Several previous studies have proposed methods to monitor cough frequency using a microphone [15-22], but not to monitor cough ability. If the assessment of the cough ability by cough sounds is feasible, it can be applied to patients in

whom obtaining cough peak flow measurements using the current method is difficult. However, the relationship between cough flow and cough sounds has not yet been clarified.

This study tested the hypothesis that cough sounds are associated with cough flow, and we propose a cough flow prediction model using cough sounds based on our previous work [23]. Experiments were performed to determine the optimal cough sound measurement method and to investigate the influence of microphone type and participant height and gender on the accuracy of the estimated CPF via cough sounds (CPS) in young healthy participants. The effectiveness of the proposed model was also verified by comparison with polynomial functions.

2. Materials and Methods

2.1. Ethics statement

This study was conducted in accordance with the amended Declaration of Helsinki. The Hiroshima Cosmopolitan University Institutional Review Board (No. 2015031) approved the protocol, and written informed consent for study participation and publication of identifying information/images in an online open-access publication was obtained from all participants.

2.2. Participants

A total of 73 young healthy participants who were screened for the absence of pulmonary illness (forced expiratory volume in 1 second of at least 70% of predicted) with no history of pulmonary disease were included in this study. The participants were non-smokers, were taking no long-term prescription medications, and did not have any other medical illnesses. The mean ± standard deviation age of the participants was 21.0 ± 1.2 years (range, 20 to 28 years). Table 1 shows the baseline characteristics of the participants.

Table 1. Characteristics of the participants.

Variable	Experiment 1 (n = 33)	Experiment 2 (n = 7)	Experiment 3 (n = 33)
Age, years	20.7 ± 1.0	22.0 ± 2.8	21.3 ± 0.4
Male gender, n	21	5	20
Height, cm	167 ± 7.9	167 ± 7.5	165 ± 8.4
Body weight, kg	61.5 ± 12	58.7 ± 9	58.5 ± 11
BMI, kg/m2	21.9 ± 3.2	22.0 ± 2.8	21.3 ± 0.5

Values presented as means ± standard deviations.

2.3. Cough flow measurements

Figure 1a shows the cough flow measurement method that was performed with the participants in a sitting position for all experiments. Participants wore a face mask with the flow sensor (Mobile Aeromonitor AE-100i; Minato Medical Science Co., Ltd., Osaka, Japan) attached. The measurement range of the flow sensor was 0–840 L/min, and the measurement accuracy was within 3% of the indicated value. The cough flow signal was digitized using a 16-bit analogue-to-digital converter (PowerLab 16/35, ADInstruments, Inc., Dunedin, New Zealand) at a 100-kHz sampling rate set by analytical software (LabChart version 8, ADInstruments, Inc.). CPF was calculated from the maximal value of the cough flow data obtained under the different experimental conditions.
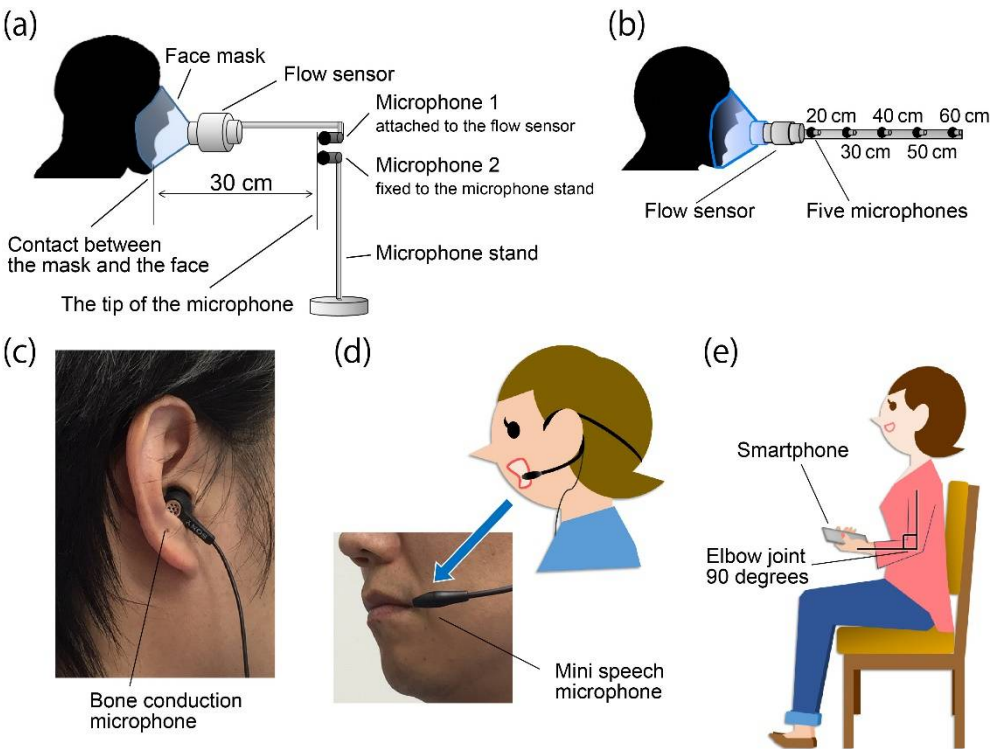
Figure 1. Experimental methods. (a): Experiment 1 method. The cough flow measurement is performed with the participants in a sitting position. The participants wear a face mask with an attached flow sensor. Two microphones are installed 30 cm from the point of face mask contact with the face. Microphone 1 is attached to the flow sensor, and microphone 2 is fixed to the microphone stand. (b): Experiment 2 method. each microphone is installed 20 cm, 30 cm, 40 cm, 50 cm, and 60 cm away from the point of face mask contact with the face. (c): Bone conduction microphone. The bone conduction microphone was used in experiment 3 and fixed at the right external auditory canal. (d): Mini speech microphone. The mini speech microphone was used in experiment 3. (e): Smartphone microphone: The smartphone microphone was used in experiment 3.

2.4. Cough sound measurements

Figure 1 shows the cough sound measurement method that was performed with the participants in a sitting position for all experiments.

Experiment 1. Cough sounds were measured using two microphones (AT9903, Audio-Technica Corporation, Tokyo, Japan), simultaneously with cough flow. The sensitivity of the microphones was -42 dB (0 dB = 1 V/1 Pa, 1 kHz). Both microphones were installed 30 cm away from the point of face mask contact with the face, but by different installation methods to test their efficacy; that is, microphone 1 was fixed to the flow sensor [24], and microphone 2 was fixed to the microphone stand, as shown in Figure 1a.

Experiment 2. Cough sounds were simultaneously measured using five microphones of the same type as in experiment 1. Each microphone was installed at 20 cm, 30 cm, 40 cm, 50 cm, and 60 cm away from the point of face mask contact with the face (Figure 1b).

Experiment 3. Cough sounds were measured using three types of microphones. To measure cough sounds via bone conduction from the right external auditory canal, an electret condenser microphone (ECM-TL3; Sony Corporation, Japan) (bone conduction microphone) was attached to the right ear canal (Figure 1c). The sensitivity of the microphone was -35.0 dB (0 dB = 1 V/1 Pa, 1 kHz). A headset mini speech microphone (ECM-322BMP; Sony Corporation, Japan) (mini speech microphone) was attached to the left ear (Figure 1d). The sensitivity of the microphone was -42.0 dB (0 dB = 1 V/1 Pa, 1 kHz). The smartphone (iPhone 6 A1586; Apple, Inc., USA) (smartphone

111 microphone) was held in the left hand while the participant bent their elbow to 90 degrees and their
112 shoulder to 0 degrees and then rotated their arm internally to 45 degrees (Figure 1e). In the same
113 manner as the cough flow method, analogue cough sound data were converted into digital signals at
114 a sampling frequency of 100 kHz and stored on a personal computer. The digitized cough sound
115 signals were bandpass filtered between 140 to 2,000 Hz to minimize artefacts caused by heart sounds
116 and muscle interference because wearable microphones were used in experiment 3. The CPSL value
117 was calculated from the maximal value of the cough sound data obtained under the different
118 experimental conditions using LabChart version 8 software.

119 *2.5. Experimental protocols*

120   *Experiments 1 and 2.* Participants' voluntary coughs were measured under three different
121 conditions: five times with maximal effort from a maximal inspiratory level; five times with maximal
122 effort from a resting inspiratory level; and five times with slight effort from a resting inspiratory level.
123 Thus, a total of 15 cough flows and cough sounds per participant were measured simultaneously.
124 Therefore, the total cough sample size was 495. The participants were allowed to cough at their own
125 arbitrary intervals.
126   *Experiment 3.* After providing sufficient instructions regarding the cough method to the
127 participants, maximal voluntary coughing was performed three times. The participants had enough
128 rest between each trial to reduce the effects of fatigue. CPF and CPSL were determined as the
129 maximum value of each set of measured values.

130 *2.6. Statistical analysis*

131   The relationship between CPF and cough sound was assumed to be in a form of exponential
132 function, as in the following equation:

$$CPF = \alpha\left(e^{\beta \cdot CPSL} - 1\right), \tag{1}$$

133   where α and β are constants, and *CPSL* is the maximum cough sound. The Levenberg-Marquardt
134 method was used to determine the coefficients in the proposed model; equation (1) and the 95% CI
135 of each coefficient, respectively. The Spearman's rank correlation coefficient analysis was used to
136 analyse the relationship between CPS and CPF and the estimation accuracy of CPS. In addition, the
137 absolute error was calculated from CPS and CPF. Absolute reliability was investigated using the
138 Bland-Altman analysis method to detect systematic bias, such as fixed and proportional bias. The
139 Friedman test was used to compare the absolute error of the different distances from the sound source
140 to the microphone and the different microphone types. The Mann-Whitney U test was used to
141 compare the absolute error between the gender groups. The Bonferroni test was used for the post hoc
142 analysis.
143   *The effect of participant's height on the proposed model.* We hypothesized that coefficient α
144 proportionally increases with height, and we represented α using a linear term related to height, as
145 in the following equation:

$$CPF = (\alpha_1 \cdot h + \alpha_2)\left(e^{\beta \cdot CPSL} - 1\right), \tag{2}$$

146 where h represents participant's height, and α_1, α_2 and β are constants. The data from microphone 1
147 used in experiment 1 were also used for this experiment.
148   *The effect of participant's gender on the proposed model.* To determine the effect of gender on CPS,
149 we divided participants into male and female groups, and coefficients α and β were calculated for
150 each group using the Levenberg-Marquardt method. Moreover, Mann-Whitney's U test was used to
151 compare the coefficients between the two groups. The data recorded from microphone 1 in
152 experiment 1 were used for this analysis. Finally, we verified the efficacy of the proposed model by
153 comparison with first- to fourth-order polynomial functions, as in the following equation:

$$CPF = \alpha_3 \cdot CPSL, \tag{3}$$

$$CPF = \alpha_4 \cdot CPSL^2 + \alpha_5 \cdot CPSL, \tag{4}$$

$$CPF = \alpha_6 \cdot CPSL^3 + \alpha_7 \cdot CPSL^2 + \alpha_8 \cdot CPSL, \tag{5}$$

$$CPF = \alpha_9 \cdot CPSL^4 + \alpha_{10} \cdot CPSL^3 + \alpha_{11} \cdot CPSL^2 + \alpha_{12} \cdot CPSL, \tag{6}$$

154 where $\alpha_{3\text{-}12}$ are constants. The Levenberg-Marquardt method was also used to determine the
155 coefficient in the equations and the coefficient of determination, and the 95% CIs were calculated.
156 The data from microphone 1 in experiment 1 were used for this analysis.
157   All statistical tests in this paper assumed a significance level of 5%, and analyses were performed
158 using G*power (version 3.1.9.2; University Kiel, Germany) and SPSS Statistics (version 24.0; IBM,
159 Chicago, IL, USA).

160 **3. Results**

161 *3.1. Experiment 1: Relationships between CPF and CPSL and verification of the microphone installation*
162 *method*

163   Figure 2 shows examples of cough flow and cough sounds measured by microphones 1 and 2
164 (Figure 1a). Although the cough flow and cough sounds were measured using different methods,
165 both responded to the initiation of the participant cough almost simultaneously. Figure 3a shows the
166 relationship between CPF and CPSL measured by microphone 1 attached to the flow sensor. The
167 coefficients of equation (1), determined by the Levenberg-Marquardt method, are as follows: $\alpha = 5.67$
168 (95% confidence internal (CI): 4.557 to 6.784) and $\beta = 0.044$ (95% CI: 0.042 to 0.046); the determination
169 coefficient was 0.843. Therefore, the following estimation formula could be derived from *CPSL*
170 measured by microphone 1:

$$CPF = 5.67(e^{0.044CPSL} - 1). \tag{7}$$

171 Figure 3b shows the relationship between CPF and CPS, which confirmed a significant positive
172 correlation (r = 0.920; p < 0.001; power, 100%).

173
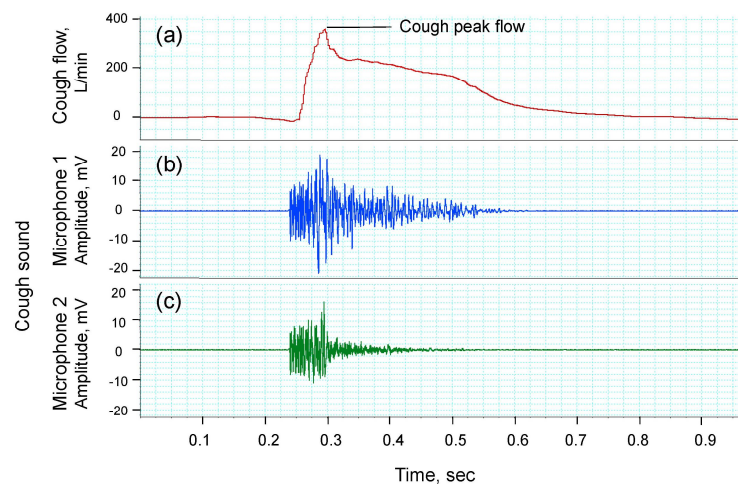
174 **Figure 2.** Examples of cough flow and cough sounds measured by microphones 1 and 2. (a):
175 Experimental data of cough flow signals in experiment 1. CPF, cough peak flow; (b): Experimental
176 data of cough sound signals measured by microphone 1 attached to the flow sensor in experiment 1.
177 (c): Experimental data of cough sound signals measured by microphone 2 fixed to the microphone
178 stand in experiment 1.

179

(a)   (b)
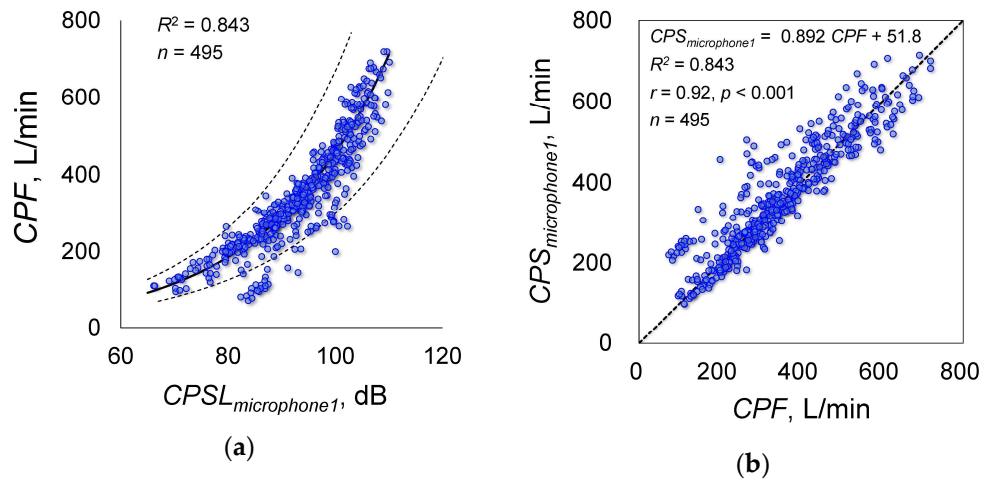
Figure 3. Estimation accuracy of equation (7) calculated from the experimental data measured by microphone 1 attached to the flow sensor. (**a**): Relationship of *CPF* and *CPSL$_{microphone1}$*. The solid lines represent the regression curves derived by fitting the coefficients in the proposed model using the Levenberg-Marquardt method based on *CPF* and *CPSL$_{microphone1}$*. The dotted lines represent 95% confidence bands. *CPF*, cough peak flow; *CPSL$_{microphone1}$*, cough peak sound pressure level by microphone 1. (**b**) Relationship between *CPF* and *CPS$_{microphone1}$*. *CPS$_{microphone1}$*, estimated cough peak flow calculated from *CPSL$_{microphone1}$*.

In case of the experimental data measured by microphone 2 fixed to the microphone stand (Fig 1a), the Levenberg-Marquardt method showed that the coefficients obtained are as follows: $\alpha = 38.731$ (95% CI: 24.071 to 53.391), $\beta = 0.026$ (95% CI: 0.023 to 0.030); the determination coefficient was 0.455. The Spearman's rank correlation coefficient analysis showed a significant positive correlation between CPF and CPS ($r = 0.699$; $p < 0.001$; power, 100%). The Bland-Altman plot of CPF and CPS did not show fixed bias but did show proportional bias ($r = -0.453$; $p < 0.001$; power, 100%). Thus, the estimation accuracy of equation (7) calculated from the experimental data measured by microphone 1 was higher than that measured by microphone 2.

3.2. Experiment 2: Effects of microphone distance from the sound source on estimation accuracy.

The cough sounds were measured by five microphones in the same model as experiment 1. These microphones were installed at 20 cm, 30 cm, 40 cm, 50 cm, and 60 cm from the point of face mask contact with the face of the participant (Figure 1b). Figure 4 shows the results of the experimental data for each distance and the correlation analysis between CPF and CPS. The determination coefficients were 0.864 for 20 cm, 0.841 for 30 cm, 0.619 for 40 cm, 0.556 for 50 cm, and 0.554 for 60 cm. The correlation coefficients were 0.903 ($p < 0.001$; power, 100%) for 20 cm, 0.909 ($p < 0.001$; power, 100%) for 30 cm, 0.775 ($p < 0.001$; power, 100%) for 40 cm, 0.76 ($p < 0.001$; power, 100%) for 50 cm, and 0.747 ($p < 0.001$; power, 100%) for 60 cm. The absolute errors were 40.5 ± 26.7 L/min for 20 cm, 41.3 ± 30.6 L/min for 30 cm, 64.9 ± 46.2 L/min for 40 cm, 70.7 ± 49.0 L/min for 50 cm, and 72.0 ± 47.5 L/min for 60 cm. Figure 5 shows the results of the Friedman and Bonferroni tests between the absolute error of each distance. The Friedman test showed that there was a significant difference among the absolute errors ($p < 0.001$). The Bonferroni test showed that the absolute errors were significantly lower for 20 cm and 30 cm than for 40 cm, 50 cm, and 60 cm ($p < 0.001$).
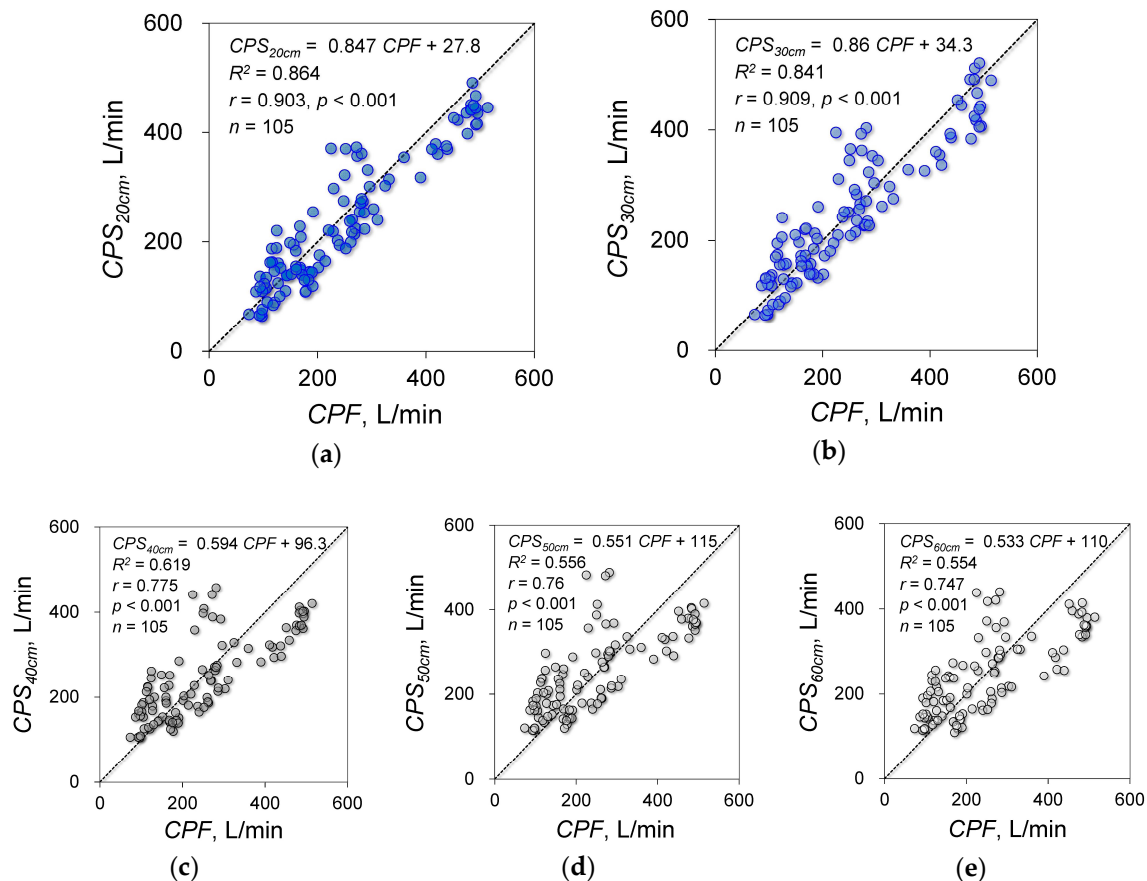
Figure 4. Estimation accuracy in each measurement condition. (a)-(e): Scatter plots of the measured data and the regression results of the proposed model: $CPSL_{20cm-60cm}$, cough peak sound pressure level measured by each microphone installed 20 cm, 30 cm, 40 cm, 50 cm, and 60 cm from the point of face mask contact with the face; $CPS_{20cm-60cm}$, estimated cough peak flow calculated by $CPSL_{20cm-60cm}$. Solid lines represent regression lines derived from CPF and $CPSL$. The variation around the identity line is visibly reduced in graphs (a) and (b).
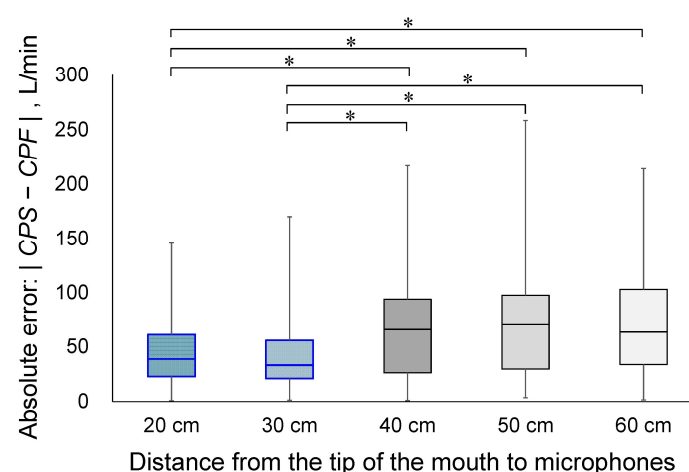

Figure 5. Comparison of the absolute error between each measurement condition. *CPF*, cough peak flow; *CPS*, estimated cough peak flow; *, *p* < 0.001.

3.3. Experiment 3: Effects of microphone type on estimation accuracy.

A total of 33 young healthy participants were included in experiment 3. Measuring cough sounds using the bone conduction microphone, the mini speech microphone, and the smartphone

222　microphone, $CPS_{bone\text{-}conduction}$, $CPS_{mini\text{-}speech}$, and $CPS_{smartphone}$ were estimated, respectively. Figure 6
223　shows the results of the experimental data measured by each microphone and the correlation and
224　regression analysis results between CPF and each CPS. The determination coefficients between CPF
225　and each CPS estimated by the bone conduction, mini speech, and smartphone microphones were
226　0.763, 0.782, and 0.641, respectively. Significant positive correlations were found between CPF and
227　each CPS (bone conduction microphone: $r = 0.895$; $p < 0.001$; power, 100%, mini speech microphone:
228　$r = 0.879$; $p < 0.001$; power, 100%, smartphone microphone: $r = 0.795$; $p < 0.001$; power, 99.9%). The
229　absolute errors were 27.3 ± 22.6 L/min, 29.9 ± 27.4 L/min, and 38.8 ± 35.7 L/min for the bone
230　conduction, mini speech, and smartphone microphones. The Friedman test showed that there were
231　no significant differences among the absolute errors ($p = 0.157$).
232

(a)　　　　　　　　　　　(b)　　　　　　　　　　　(c)
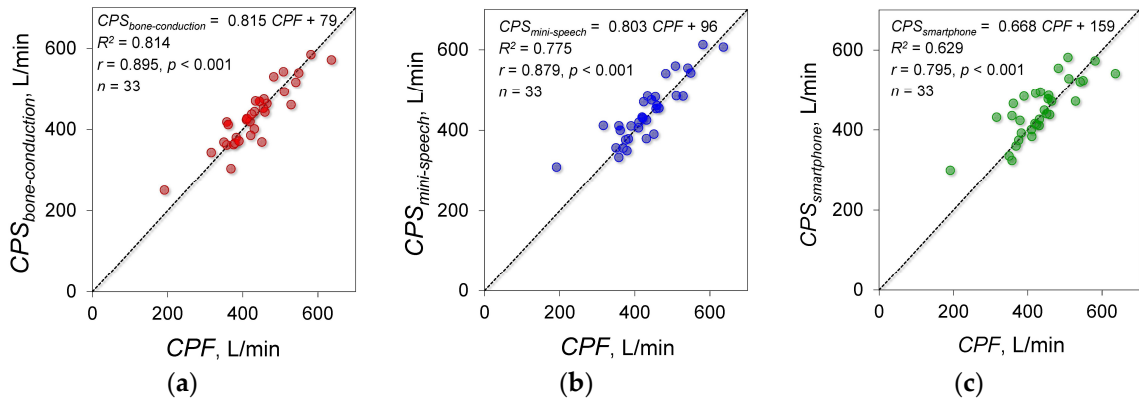
233　**Figure 6.** The results of experiment 3. *CPF*, cough peak flow; $CPS_{bone\text{-}conduction}$, estimated CPF
234　calculated from cough sound measured using the bone conduction microphone; $CPS_{mini\text{-}speech}$, estimated CPF calculated from cough sound measured using the mini speech
236　microphone; $CPS_{smartphone}$, estimated CPF calculated from cough sound measured using the
237　smartphone microphone; (a): Relationship between *CPF* and $CPS_{bone\text{-}conduction}$. (b):
238　Relationship between *CPF* and $CPS_{mini\text{-}speech}$. (c): Relationship between *CPF* and CPS_{smart}.

239

240　*3.4. Effects of participant's height on estimation accuracy.*

241　　　　To consider the effect of height on the estimation accuracy of CPF, height parameters were
242　introduced in the proposed model, such as equation (2). The coefficients $a1$, $a2$, and β were
243　determined by the Levenberg-Marquardt method using the measured data of experiment 1 measured
244　by microphone 1 attached to the flow sensor. This model yielded a determination coefficient of 0.843.
245　The determined coefficients were as follows: $a_1 = -0.001$ (95% CI: -0.012 to 0.01), $a_2 = 5.767$ (95% CI:
246　3.946 to 7.588), and $\beta = 0.042$ (95% CI, 0.04 to 0.044).

247　*3.5. Effects of gender on estimation accuracy.*

248　　　　To consider the effect of gender on the estimation accuracy of CPF, the participants were divided
249　into male and female groups, and the coefficients of the proposed model, such as equation (1), were
250　determined for the respective groups. The coefficient α values were 8.3 ± 5.8 for the male group and
251　7.5 ± 5.4 for the female group. The Mann-Whitney U test showed no significant difference in the
252　coefficient α values between the male and female groups ($p = 0.653$). The coefficient β values 0.049 ±
253　0.027 for the male group and 0.044 ± 0.01 for the female group. The Mann-Whitney U test showed no
254　significant difference in the coefficient β values between the male and the female groups ($p = 0.506$).

255　*3.6. Comparison between the proposed model and polynomial functions.*

256　　　　To demonstrate the efficacy of the proposed model, its estimation accuracy was compared with
257　the polynomial functions without intercepts, such as equations (3) to (6). The coefficients $\alpha_{3\text{-}12}$ were
258　determined by the Levenberg-Marquardt method in the same manner as in the proposed model.

Table 2 shows the determined parameters and statistical analysis results. The 95% CIs of all coefficients in equation (6) include 0, which indicates that the fourth-order polynomial function is redundant to estimate cough peak flow. Based on these results, the following analysis used our proposed model of equation (1) and equations (3) to (5). The absolute errors between CPF and CPS were 40.0 ± 41.8 L/min in the proposed model, 89.7 ± 65.2 L/min in equation (3), 43.7 ± 39.9 L/min in equation (4), and 98 ± 62.8 L/min in equation (5). The Friedman test showed that there was a significant difference among the absolute errors ($p < 0.001$). The Bonferroni test showed that the absolute error was significantly lower in the proposed model and equation (4) than in equations (3) and (5) ($p < 0.001$). In addition, Figure 7 shows the corresponding Bland-Altman plot of the proposed model and equation (4). The proposed model did not show fixed bias and proportional bias. However, equations (4) did not show fixed bias, but did show proportional bias ($r = -0.343$, $p < 0.001$).

Table 2. Relationship between cough peak flow and cough peak sound pressure level using equations (2) to (4).

Estimation equation	Coefficient	Estimated value	Standard error	95% CI Lower	95% CI Upper	Determination coefficient
Equation (3)	α_3	3.819	0.053	3.714	3.923	0.373
Equation (4)	α_4	0.117	0.003	0.111	0.124	0.822
	α_5	-7.288	0.317	-7.910	-6.665	
Equation (5)	α_6	0.002	0.000	0.002	0.003	0.843
	α_7	-0.326	0.054	-0.431	-0.220	
	α_8	13.013	2.2485	8.132	17.895	
Equation (6)	α_9	0.019	0.000	-0.015	0.052	0.844
	α_{10}	-0.005	0.007	-0.019	0.008	
	α_{11}	0.355	0.617	-0.858	1.567	
	α_{12}	-7.198	18.431	-43.412	29.016	

$n = 33$ participants.

(a)   (b)
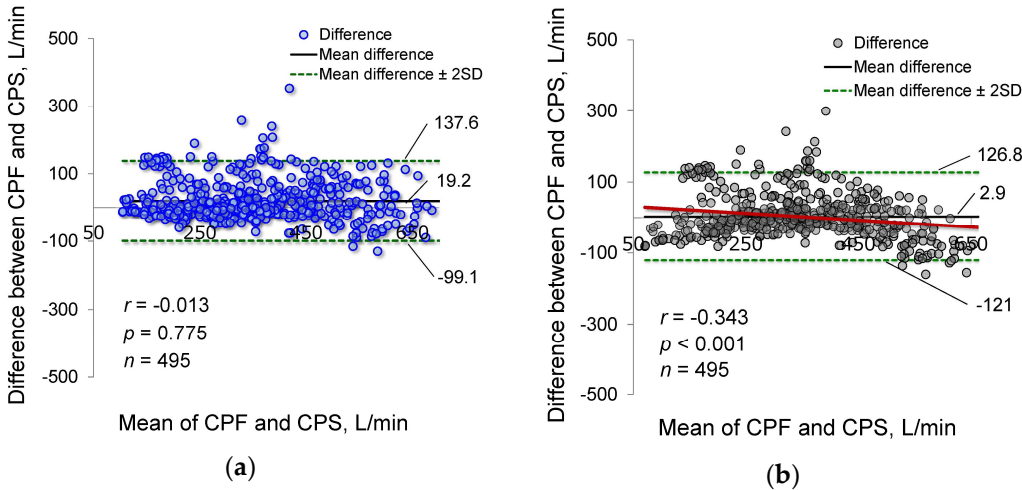
Figure 7. Bland-Altman plot of the measured and estimated cough peak flow. CPF, cough peak flow; CPS, estimated cough peak flow; (a): CPS estimated using our proposed model of equation (1); (b): CPS estimated using equation (4). Blue and black dots represent the difference between CPF and CPS. Bold black solid lines represent the mean difference between CPF and CPS. Green dotted lines represent the mean difference ± 2 standard deviation bands. Red lines represent the approximate straight line of the difference between CPF and CPS and the mean of CPF and CPS.

280   **4. Discussion**

281   To the best of our knowledge, this is the first study to develop a method for estimating cough
282   strength via cough sounds using a model represented by an exponential equation. Analysis of the
283   results of experiment 1 demonstrated that CPS calculated from the cough sound measured using
284   microphone 1 attached to a flow sensor is estimated to have high accuracy. Moreover, the CPF
285   estimation accuracy using microphone 1 is significantly higher than that using microphone 2 fixed to
286   the microphone stand. This is because microphone 1 was attached to the flow sensor, which
287   maintained a fixed distance from the vocal cords, but the distance between microphone 2, which was
288   attached to the microphone stand, and the vocal cords could be changed by inspiratory and/or
289   coughing-induced body motion. The decrease in the sound level L_p can be calculated by the distance
290   from the sound source r_1, r_2 using the following equation:

$$L_p = 20 \log\left(\frac{r_2}{r_1}\right). \tag{8}$$

291   The fact that the sound pressure level decreases with distance from the sound source indicates
292   that body motion may be a cause of artefacts and, therefore, reduces estimation accuracy. Thus, to
293   improve estimation accuracy, microphones should be installed on the body so that the microphones
294   can maintain a constant distance from the sound source.
295   In experiment 2, we found that the distance between the mouth, as a sound source, and the
296   microphone needs to be less than 30 cm. Sound propagation in a room is a combination of direct and
297   reflected sound waves from surfaces and boundaries in the room [25]. In addition, the sound
298   attenuates with increasing distance from the sound source, as shown in equation (8). When the
299   microphone is set at a distance more than 30 cm from the mouth, the measured cough sounds may
300   be influenced by sounds reflected from the walls and/or sound attenuation.
301   In experiment 3, we used three types of microphones (i.e., a bone conduction microphone, a mini
302   speech microphone, and a smartphone microphone) to measure cough sounds. The strongest
303   correlation between CPF and CPS was estimated using data obtained from the bone conduction
304   microphone. Thus, these microphones could be introduced as simple and wearable cough strength
305   measurement devices.
306   In the respiratory function test, participant height is generally used to determine the normal
307   level of respiratory function [26,27], and a relationship between CPF and height has been reported
308   [28]. Based on these previous studies, we hypothesized that height affects CPS; however, in equation
309   (2), in which the coefficient α of equation (1) was replaced by a linear function of height, the 95% CI
310   of the multiplication coefficient α_1 onto the height ranged from -0.112 to 0.02, including 0. This result
311   indicates that height has a minimal effect on the CPF estimation accuracy.
312   Previous studies have also suggested that normal respiratory function levels vary according to
313   gender [26,27], and the CPF of male participants has been shown to be significantly higher than that
314   of female participants [28]. Therefore, we hypothesized that gender can affect the coefficients in the
315   estimation equation; however, no significant difference in estimation accuracy was found between
316   male and female participants. This result demonstrates that gender also has a minimal effect on the
317   estimation accuracy when adopting the proposed model, represented by equation (1).
318   We verified the prediction equation using first- to fourth-order polynomial functions. Several
319   previous studies have reported that the relationship between air flow and breath sound amplitude is
320   linear under high flow rate conditions [29,30]. It has also been reported that the sound amplitude
321   during inspiration is proportional to the square of the air flow at the mouth [31]. Similar to these
322   previous studies, cough sounds were proportional to the square of the cough flow in our study;
323   however, a proportional bias was found in the second-order polynomial function, such as equation
324   (4). The effectiveness of the proposed model, represented by the exponential function, such as
325   equation (1), was verified by the fact that it successfully eliminated this systematic bias.
326   A major limitation of this study is that we did not fully consider the effect of age since the study
327   participants were young healthy volunteers. In the respiratory function test, participant age is
328   generally used to determine the normal level of respiratory function [26,27], and a relationship

between CPF and age has been reported [28]. Therefore, the effects of age should be investigated in future studies.

5. Conclusions

This study has developed a system for assessing the cough ability via cough sounds. Future studies should verify whether age influences the accuracy of the prediction model. Since cough sounds can be recorded conveniently with the microphones used in this study, a practical device for assessing cough ability could be developed by employing the proposed method.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Chatwin, M.; Toussaint, M.; Goncalves, M.R.; Sheers, N.; Mellies, U.; Gonzales-Bermejo, J.; Sancho, J.; Fauroux, B.; Andersen, T.; Hov, B*., et al.* Airway clearance techniques in neuromuscular disorders: A state of the art review. *Respir Med* **2018**, *136*, 98-110.

2. Srour, N.; LeBlanc, C.; King, J.; McKim, D.A. Lung volume recruitment in multiple sclerosis. *PloS one* **2013**, *8*, e56676.

3. LoMauro, A.; Aliverti, A.; Mastella, C.; Arnoldi, M.T.; Banfi, P.; Baranello, G. Spontaneous breathing pattern as respiratory functional outcome in children with spinal muscular atrophy (sma). *PloS one* **2016**, *11*, e0165818.

4. Benditt, J.O.; Boitano, L.J. Pulmonary issues in patients with chronic neuromuscular disease. *Am J Respir Crit Care Med* **2013**, *187*, 1046-1055.

5. Sancho, J.; Servera, E.; Diaz, J.; Marin, J. Predictors of ineffective cough during a chest infection in patients with stable amyotrophic lateral sclerosis. *Am. J. Respir. Crit. Care Med.* **2007**, *175*, 1266-1271.

6. Finder, J.D.; Birnkrant, D.; Carl, J.; Farber, H.J.; Gozal, D.; Iannaccone, S.T.; Kovesi, T.; Kravitz, R.M.; Panitch, H.; Schramm, C*., et al.* Respiratory care of the patient with duchenne muscular dystrophy: Ats consensus statement. *Am J Respir Crit Care Med* **2004**, *170*, 456-465.

7. Bach, J.R.; Saporito, L.R. Criteria for extubation and tracheostomy tube removal for patients with ventilatory failure. A different approach to weaning. *Chest* **1996**, *110*, 1566-1571.

8. Su, W.L.; Chen, Y.H.; Chen, C.W.; Yang, S.H.; Su, C.L.; Perng, W.C.; Wu, C.P.; Chen, J.H. Involuntary cough strength and extubation outcomes for patients in an icu. *Chest* **2010**, *137*, 777-782.

9. Duan, J.; Zhou, L.; Xiao, M.; Liu, J.; Yang, X. Semiquantitative cough strength score for predicting reintubation after planned extubation. *American journal of critical care : an official publication, American Association of Critical-Care Nurses* **2015**, *24*, e86-90.

10.   Duan, J.; Liu, J.; Xiao, M.; Yang, X.; Wu, J.; Zhou, L. Voluntary is better than involuntary cough peak flow for predicting re-intubation after scheduled extubation in cooperative subjects. *Respir Care* **2014**, *59*, 1643-1651.

11.   Smailes, S.T.; McVicar, A.J.; Martin, R. Cough strength, secretions and extubation outcome in burn patients who have passed a spontaneous breathing trial. *Burns : journal of the International Society for Burn Injuries* **2013**, *39*, 236-242.

12.   Bach, J.R. Amyotrophic lateral sclerosis: Predictors for prolongation of life by noninvasive respiratory aids. *Arch Phys Med Rehabil* **1995**, *76*, 828-832.

13.   Bach, J.R.; Ishikawa, Y.; Kim, H. Prevention of pulmonary morbidity for patients with duchenne muscular dystrophy. *Chest* **1997**, *112*, 1024-1028.

14.   Bai, L.; Duan, J. Use of cough peak flow measured by a ventilator to predict re-intubation when a spirometer is unavailable. *Respir Care* **2017**, *62*, 566-571.

15.   Larson, S.; Comina, G.; Gilman, R.H.; Tracey, B.H.; Bravard, M.; Lopez, J.W. Validation of an automated cough detection algorithm for tracking recovery of pulmonary tuberculosis patients. *PloS one* **2012**, *7*, e46229.

16.   Morice, A.H.; Fontana, G.A.; Belvisi, M.G.; Birring, S.S.; Chung, K.F.; Dicpinigaitis, P.V.; Kastelik, J.A.; McGarvey, L.P.; Smith, J.A.; Tatar, M., *et al.* Ers guidelines on the assessment of cough. *Eur. Respir. J.* **2007**, *29*, 1256-1276.

17.   Sumner, H.; Woodcock, A.; Kolsum, U.; Dockry, R.; Lazaar, A.L.; Singh, D.; Vestbo, J.; Smith, J.A. Predictors of objective cough frequency in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* **2013**, *187*, 943-949.

18.   Ing, A.J.; Ngu, M.C.; Breslin, A.B. Pathogenesis of chronic persistent cough associated with gastroesophageal reflux. *Am J Respir Crit Care Med* **1994**, *149*, 160-167.

19.   Lee, K.K.; Matos, S.; Evans, D.H.; White, P.; Pavord, I.D.; Birring, S.S. A longitudinal assessment of acute cough. *Am J Respir Crit Care Med* **2013**, *187*, 991-997.

20.   Birring, S.S.; Matos, S.; Patel, R.B.; Prudon, B.; Evans, D.H.; Pavord, I.D. Cough frequency, cough sensitivity and health status in patients with chronic cough. *Respir Med* **2006**, *100*, 1105-1109.

21.   Birring, S.S.; Fleming, T.; Matos, S.; Raj, A.A.; Evans, D.H.; Pavord, I.D. The leicester cough monitor: Preliminary validation of an automated cough detection system in chronic cough. *Eur Respir J* **2008**, *31*, 1013-1018.

22.   Spinou, A.; Birring, S.S. An update on measurement and monitoring of cough: What are the important study endpoints? *J Thorac Dis* **2014**, *6*, S728-734.

23.   Umayahara, Y.; Soh, Z.; Ozaki, T.; Murakami, T.; Otsuka, A.; Tsuji, T. In Ability to cough can be evaluated through cough sounds: An experimental investigation of effects of microphone type on accuracy, *2017 IEEE/SICE International Symposium on System Integration (SII)*, 11-14 Dec. 2017, **2017**; pp 936-941.

24.   Toop, L.J.; Dawson, K.P.; Thorpe, C.W. A portable system for the spectral analysis of cough sounds in asthma. *The Journal of asthma : official journal of the Association for the Care of Asthma* **1990**, *27*, 393-397.

413   25.   Shafieian, M.; Kashani, F.H. Effect of diffusive and nondiffusive surfaces
414   combinations on sound diffusion. *Acoustical Physics* **2010**, *56*, 342-347.
415   26.   Baldwin, E.D.; Cournand, A.; Richards, D.W., Jr. Pulmonary insufficiency;
416   physiological classification, clinical methods of analysis, standard values in normal
417   subjects. *Medicine* **1948**, *27*, 243-278.
418   27.   Berglund, E.; Birath, G.; Bjure, J.; Grimby, G.; Kjellmer, I.; Sandqvist, L.;
419   Soderholm, B. Spirometric studies in normal subjects. I. Forced expirograms in
420   subjects between 7 and 70 years of age. *Acta medica Scandinavica* **1963**, *173*, 185-
421   192.
422   28.   Bianchi, C.; Baiardi, P. Cough peak flows: Standard values for children and
423   adolescents. *American journal of physical medicine & rehabilitation / Association of
424   Academic Physiatrists* **2008**, *87*, 461-467.
425   29.   Kraman, S.S. The relationship between airflow and lung sound amplitude in normal
426   subjects. *Chest* **1984**, *86*, 225-229.
427   30.   Dosani, R.; Kraman, S.S. Lung sound intensity variability in normal men. A contour
428   phonopneumographic study. *Chest* **1983**, *83*, 628-631.
429   31.   Shykoff, B.E.; Ploysongsang, Y.; Chang, H.K. Airflow and normal lung sounds. *The
430   American review of respiratory disease* **1988**, *137*, 872-876.
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