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공학석사 학위논문

일차원 합성곱 신경망을 이용한 동맥압 파형으로 일회박출량 변화도 예측

Estimated Stroke Volume Variation using 1-D Convolutional Neural Network from Arterial Blood Pressure

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이 논문을 공학석사학위 논문으로 제출함

2020 년 8 월

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김재만의 공학석사 학위 논문을 인준함

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감사의 글

대학원 석사과정 동안 저를 도와주신 모든 분들께 이글을 통해 감사의 말씀을 전합니다.

우선 석사과정 동안 부족한 저에게 많은 지원과 지도를 해주신 김성훈 교수님께 감사드립니다. 그리고 부족한 논문을 심사해주시고 조언과 격려를 해주신 황규삼 교수님, 신원정 교수님께 감사의 말씀을 전합니다.

또한 연구 진행과정동안 많이 도와주신 권혜미 선생님과 논문을 작성할 때 도와주셨던 서우영 박사님 감사합니다. 그리고 연구실 생활을 같이한 분들에게 모두 감사합니다.

[국문 요약]

Estimated Stroke Volume Variation using 1-D Convolutional Neural Network from Arterial Blood Pressure

울산대학교 대학원

의공학과

김 재 만

Stroke volume Variation (SVV, 일회박출량 변화도)는 전신 마취 수술에서 환자의 수액 반응성을 판단하는 중요한 지표이다. 하지만 SVV 를 측정하는 장비는 공간을 차지하고 가격이 비싸서 모든 환자에게 적용하기 힘들다. 이 연구는 인공지능 모델을 이용하여 SVV 를 측정하여 현재 장비의 문제점을 극복하고자 하였다.

총 557 명 환자를 대상으로 진행했으며 training (210 명), validation (217 명), 그리고 test (130 명) 세트로 나누어서 학습을 진행하였다. 인공지능 모델 입력은 10 초의 동맥압 파형 (Arterial Blood Pressure, ABP)을 2 초마다 기존 장비에서 측정된 SVV 값과 매칭하여 구성하였다. Convolutional Neural Networks (CNN)을 이용해서 전처리, 다중채널, 차원축소의 개선으로 모델을 향상시켰다.

인공지능 모델을 학습한 결과를 기존 장비의 값과 통계적으로 비교하였다. 처음에는 작은 데이터셋에서 모델 개선을 진행하였다. 기본 모델은 상관 관계가 0.66, 평균 제곱 에러가 22.86 이 나왔고, 전처리와 차원축소를 개선한 모델은 상관 관계가 0.91, 평균 제곱 에러가 6.92 로 향상되었다. 전체 데이터셋에서는 1 개 신호만 사용했을 때는 상관 관계가 0.91, 평균 제곱 에러는 4.74 로 결과가 낮았고, 3 개 채널을 사용한 모델은 상관관계가 0.95, 평균 제곱 에러가 2.13 으로 높은 정확도를 보였다.

우리는 인공지능 모델을 이용해서 기존 장비의 환자 정보 이슈를 극복하였다. 또한 인공지능 모델을 이용해서 장비의 비용, 공간 등의 한계를 극복하여 더 많은 환자들에게 수액 투여 관리를 받을 수 있게 될 것이다.

목 차

그 림 목 차

표 목 차

INTRODUCTION

The anesthesiologist looks at various surgical indicators to determine the administration of fluid in general anesthesia surgery. Among them, stroke volume variation (SVV) has been used as a hemodynamic monitoring indicator to predict fluid reactivity in patients with mechanical ventilation. [1]. Fluid monitoring using SVV is essential for many bleeding surgical patients. Various medical papers the use of SVV to improve the prognosis of patients. [2, 3, 4]

SVV can be measured accurately using echocardiography, but they are measured using Edward's FloTrac equipment in surgery. FloTrac is a real-time analysis of arterial pressure waveforms for continuous monitoring of the patient's hemodynamic state and evaluates arterial tree impedance by calculating heart performance using Khi -X. Therefore, the device is ready to use after obtaining the demographics values and no external calibration is necessary [5]. However, FloTrac has various problems. The price of equipment is high and disposable medical supplies is required for each operation. Nevertheless, SVV of FloTrac is measured around and can be affected by damping, reflecting waves, and vascular tone. [6]. The operating room lacks a place because it has various anesthesia equipment. it's hard to bring equipment to the operation room in case of an emergency.

Recently, artificial intelligence techniques have developed in many areas [7, 8]. In particular, a deep learning model that requires a lot of computation has developed rapidly as hardware advances. Recently, many results have been reported in the medical field, including corneal examinations, brain tumor tests, and chest tumor tests. [9,10,11].

Many of deep learning techniques shows improved performance compared by previous method from predicted classification and regression models. Convolutional Neural Networks is one of the most typical and successful deep learning models in medical imaging [12, 13]. Recently, Reports of prediction clinical outcomes published papers using the CNN model [14]. Recently, it has also been used in bio-signal areas such as arrhythmia detection models [15, 16]. However, deep learning has not been used much in the field of anesthesia, and guidelines for models have not been established yet.

A deep learning model can overcome problems and limitations of existing equipment in predicting SVV. First, it can be freed from the cost, space aspect. If you just connect the line to the existing equipment, you can predict it with a mobile device.

In this study, we proposed SVV from the CNN model using arterial blood pressure waveform in general anesthesia operation patients. Comparing the SVV of model and the SVV of FloTrac, we confirmed that our model is competitive.

METHODS

Data preparation

This observational study was approved by Asan Medical Center Institutional Review Board (No. 2018-1163), and written informed consent was waived from the patients. Medical data recorded 624 general anesthesia patients from February 2018 to February 2019 in our institution. According to the Asan Medical Center standard protocol, biometric data of patients recorded during anesthesia surgery were collected. Anesthesia was induced with thiopental sodium, fentanyl, and vecuronium. After intubation, anesthesia was maintained with sevoflurane or desflurane in a mixture of 50% oxygen/air. The vecuronium and fentanyl were continuously infused. The hemodynamic parameters including radial and femoral arterial pressure and electrocardiogram (ECG), core temperature, pulse oximetry, and capnometer were constantly monitored. SVV was continuously monitored using FloTrac (Edwards Lifescience, USA). Severe patients use femoral vein catheterization and Swan-Ganz for monitoring inferior vena cava (IVC) pressure and pulmonary arterial pressure (PAP).

Data collection used computer application of medical record system. We collected all patients vital parameters including ECG, arterial blood pressure (ABP), central venous pressure (CVP), PAP, HR, and all of the parameters during surgery using data acquisition software named Vital Recorder [17].

Convolutional Neural Network (CNN) and Model Improvements

The observation that a neuron in the brain looks at each different part of the brain when a cat looks at an object led to the birth of the Convolutional Neural Network (CNN). [18] Through these observations, they came up with the idea that high-level neurons are based on the output of neighboring low-level neurons. LeNet-5 first used CNN to recognize handwritten letters [19]. These days, the CNN model solved various problems of image segmentation and classification in medical images [20].

CNN models have been carried out in the neural network, including the classification of vital signs for medical use. [21, 22]. The CNN model has benefited from training speed and comparatively wide feature extraction. And Recurrent Neural Networks (RNN) model is also widely used in the field of biometric signals [24]. However, research suggests that the RNN model will not surpass the CNN model in signal data, even if the performance difference is not significant. [25]. Most CNN models do not have guidelines for medical vital signals. Then, we built a customized CNN model as follows. Inputs should be set so that information on signals can be calculated well. The SVV is known as involved in differ of respiration cycle to the ABP waveform. Model input vectors have to include more than 1 cycle of respiration from the ABP waveform. So, input sequence is 10 sec obtained at 100Hz sampling rates. This model structure based on the CNN model reference by VGGNET [26]. For setting up hyperparameters on CNN models, see the temporal convolutional networks experimental guidelines [27]. Also, a model idea originally proposed on the SH-Moon et al [28]. We Improve the model to better performance. Input data for model overlap 8 seconds for augmentation. Our model composed a model using a convolutional stride layer whenever 2 layers instead of max-pooling layer to dimension reduction [29]. There are a total of 16 blocks and fully connected layers predict SVV value. Our model structure is shown in Figure 1. The loss function evaluated mean squared error(MSE) from predicted SVV and device SVV parameter. This model used Adam optimizer and was implemented by Keras library (https://github. com/keras-team/keras) and Python 3.6.

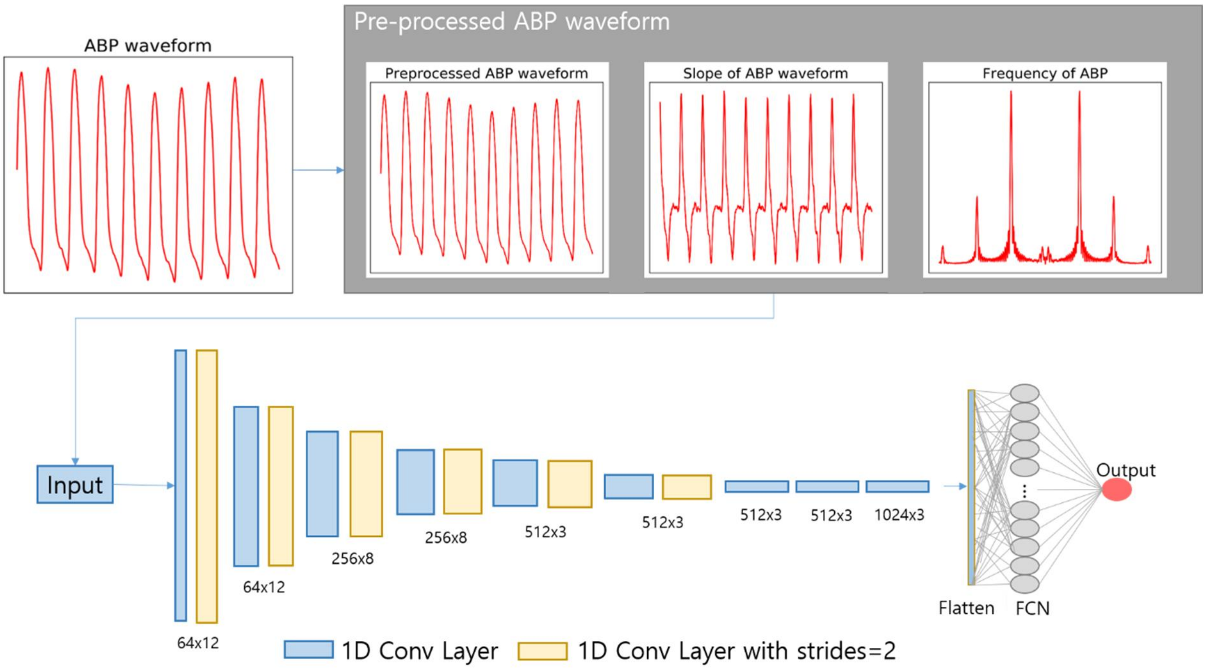

Figure 1. Convolutional neural network (CNN) model customized this project. Input pre-processed 10 seconds of arterial blood pressure (ABP) waveform into 3 channels. The inputs consist of pre-processed, frequency, and slope of ABP waveform. The model consists of 15 CNN layers and applies stride every second time.

Dataset, Pre-processing and Model Training

Totally 624 patients, 19 patients were excluded due to severe arrhythmia such as arterial fibrillation, and 48 patients with short time or noise recorded were also excluded. Finally, 557 patients were enrolled in a deep learning model dataset. Patients were split into Training set (n=210, 2018.02.01 ~ 07.31), Validation set (n=217, 2018.08.01 ~ 12.31), Test set (n=130, 2019.01 ~ 02.28). Patient distribution was adjusted by period and data set ratio. We recorded parameters measured Bx50 and FloTrac of the general medical devices. A data set concludes ABP waveform and SVV values during full-time surgery. The data set is reconstructed with ABP waveform and SVV values for 10 seconds. If there is a noise section in the ABP waveform, it is statistically detected and excluded. The data set consists of three channels. The one of input channels is the ABP waveform removed direct current (DC) offset using a digital high pass filter above the 0HZ. The baseline of the ABP waveform was moved to zero by the removal of the DC offset. This pre-processing helps deep learning model concentrate ABP forms and variance. Other input data are frequency data from 1 to 12.2 Hz on ABP waveforms using Fast-Fourier Transform. The last input data is the differential value of the ABP signal. This allows us to see the slope of ABP. Output is the SVV value learned using SVV of FloTrac. We trained a deep learning model using a GPU server with 4 GTX-1080Ti GPUs.

Statistical analysis

Variables displayed a number (percentage), average ± standard deviation, or median number (range of quartile). The intergroup analysis was performed using the student's t-test, Mann-Whitney U test, Logistic regression, the analysis of variance, or Kruskal-Wallis test for continuous variables, χ^2 test, or accurate test for categorical variables in Fisher. The mean squared error (MSE) and mean absoluted error (MAE) were calculated difference between values. Also, the relationship was evaluated using linear regression. The Bland-Altman plot was used to calculate the matching limits and deflection [E]. Trend analysis was performed using quadrants. In the paper, a margin of error of 5% was used to calculate the concordance rate. All variables were compared between FloTrac and DL models as previously explained statistic method. To evaluate the estimated model, the statistic results built Python 3.6 of programming language. Scikit-learn (https://github.com/scikit-learn/scikit-learn). Scikit-learn package evaluated Mean Absolute Error (MAE) and Mean Squared Error (MSE).

RESULTS

The patients of characteristics are displayed in Table 1. Patient characteristics did not differ depending on training, verification, and statistical test sets. The total 8,512,564 data (3,620,386 Training data, 3,944,224 Validation data and 947,954 Test data) records for 2,364 hours were used in this study. Table 2 shows the hemodynamic parameters of the device in the data set. All hemodynamic parameters compared in the data set.

Table 1. Patient characteristics in study.

	Training set (N=210)	Validation (N=217)	Testing set (N= 130)	Total set (N=557)	*P*-value
Demographics					
Age (yrs)	58 (49-63)	56 (45-63)	56 (41-64)	57 (47-63)	0.166
Sex (male)	145 (69.0)	154 (71.0)	82 (63.1)	381 (68.4)	0.300
Weight (kg)	65 ± 12	67 ± 13	64 ± 12	66 ± 13	0.021
Height (cm)	166 (160-171)	167 (160-172)	166 (160-170)	166 (160-172)	0.134
Body mass index (kg/m^2)	23.4 (21.1-26.2)	24.0 (21.6-26.8)	23.4 (21.6-25.4)	23.6 (21.3-26.2)	0.120
ASA classification					<0.001
1	12 (5.7)	8 (3.7)	23 (17.7)	43 (7.7)	
2	63 (30.0)	68 (31.3)	68 (52.3)	199 (35.7)	
3	111 (52.9)	115 (53.0)	38 (29.2)	264 (47.4)	
4	18 (8.6)	25 (11.5)	0 (0.0)	43 (7.7)	
5	6 (2.9)	1 (0.5)	1 (0.8)	8 (1.4)	
Underlying disease					
Diabetes mellitus	55 (26.2)	56 (25.8)	26 (20.0)	137 (24.6)	0.379
Hypertension	63 (30.0)	69 (31.8)	32 (24.6)	164 (29.4)	0.355
Operation time, mins	779 (399-870)	755 (423-842)	430 (320-740)	733 (376-834)	<0.001
Emergency surgery	25 (11.9)	20 (9.2)	8 (6.2)	53 (9.5)	0.210
Type of Operation					
Transplant†	150 (71.4)	150 (69.1)	53 (40.8)	353 (63.4)	<0.001
Major open abdominal surgery	52 (24.8)	62 (28.6)	71 (54.6)	185 (33.2)	<0.001
Major laparoscopic abdominal surgery	2 (1.0)	4 (1.8)	4 (3.1)	10 (1.8)	0.357
Minor abdominal surgery	5 (2.4)	0 (0.0)	0 (0.0)	5 (0.9)	0.015
Others‡	1 (0.5)	1 (0.5)	2 (1.5)	4 (0.7)	0.449

Transplant†: Liver, kidney, and pancreas transplant

Others‡: Postoperative bleeding control and sternal closure

Values are expressed as the mean (±SD) or median (interquartile range) for continuous variables, and n (%) for categorical variables.

Table 2. Hemodynamic parameter trends during the operation.

	Training (n=210, 37.7%)	Validation (n=217, 38.9%)	Test (n=130, 23.4%)	Overall (n=557)	*P*-Value
Duration (min)	120,679	131,474	31,598	283,752	
Blood pressure (mmHg)					
Systolic	110.7 ± 16.8	114.2 ± 17.4	113.0 ± 18.1	112.8 ± 17.4	<0.001
Diastolic	55.2 ± 9.6	57.5 ± 9.9	56.2 ± 9.9	56.5 ± 9.8	<0.001
Heart rate (bpm)	82.0 ± 15.2	81.3 ± 16.2	82.8 ± 14.1	81.8 ± 15.5	<0.001
Stroke volume (mL/beat)	87.3 ± 29.4	86.6 ± 26.4	80.0 ± 24.2	85.2 ± 27.5	<0.001
Stroke volume index (mL/beat/m2)	50.7 ± 16.2	50.1 ± 14.5	48.8 ± 15.2	50.2 ± 15.3	<0.001
Systemic vascular resistance (dyne ·s/cm^5)	854.3 ± 354.5	880.7 ± 331.8	931.4 ± 381.0	877.6 ± 349.6	<0.001
Cardiac output (L/min)	7.0 ± 2.6	6.9 ± 2.3	6.5 ± 2.0	6.9 ± 2.4	<0.001
Stroke volume variance (%)	8.1 ± 4.9	8.1 ± 4.4	9.4 ± 5.2	8.3 ± 4.8	<0.001

Values are expressed as mean ± standard deviation or number (%). SV, SVR, SVV, SVI, CO measured by monitoring devices calculated by stroke volume using radial arterial catheter (reference data, FloTrac, Edward Lifesciences).

We changed preprocessing and dimensional reduction to improve the model in the sample set. The sample dataset has training (n:33, data:418,121) and validation set (n:14, data:204,435). The min-max normalization of data pre-processing displayed lower performance of correlation and mean squared error (r = 0.66, MSE = 22.86). The removed DC offset replaced min-max normalization strides have better performance (correlation: 0.83, MSE: 9.3). The dimension reduction replaced convolutional strides have higher performance (correlation: 0.83, 0.91, MSE: 9.3, 6.92) in Table 3.

Table 4 shows some improvements to the input ABP waveform. Our model shows different results depending on the input signal. The ABP signals and ABP signal converted to frequency show lower performance of correlation coefficients (r=0.91, 0.88). Preprocessed ABP and slope of ABP little higher performance of correlation

Table 3. Improve models in samples

Model type	Pearson correlation, r	Mean Squared Error
Minmax Normalization + max pooling	0.64	33.21
Minmax Normalization + average pooling	0.66	22.86
Minmax Normalization + convolutional strides	0.65	31.15
Removed DC offset + max pooling	0.80	9.59
Removed DC offset + average pooling	0.83	9.3
Removed DC offset + convolutional strides	0.91	6.92

Compared of typical CNN model pre-processing and dimension reduction with proposed model in samples. Conv, convolutional layer.

coefficients and errors (r=0.93, 0.93). The combined input of pre-processed signals and frequency signals has much better performance than other inputs of correlation and error (r=0.95). Figure 2. Display a representative plot of the SVV and SVV estimates of the FloTrac. Bland-Altman analysis shows a low SD of difference (Bias: -0.85, 95% CI, -2.88 ~0.71) And the concordance rate of trend analysis demonstrated a competitive rate (95.9). the concordance rate had higher pre-processing datasets than multi-channel models (96.23%, Figure 3).

Our study analysis based on mean absoluted error and mean squared error. ABP waveforms, frequency showed higher error (MAE=1.55, 2.05, MSE= 4.74, 8.62). The pre-processed and slope ABP waveforms a little lower error (MAE=1.30, 1.38, MSE=4.08, 4.59) however, combined pre-processed and slope ABP and all combined input vectors show lower error (MAE: 1.24, 1.01, MSE: 3.18, 2.13). The results showed that changed and combined input signals contributed to improved performance.

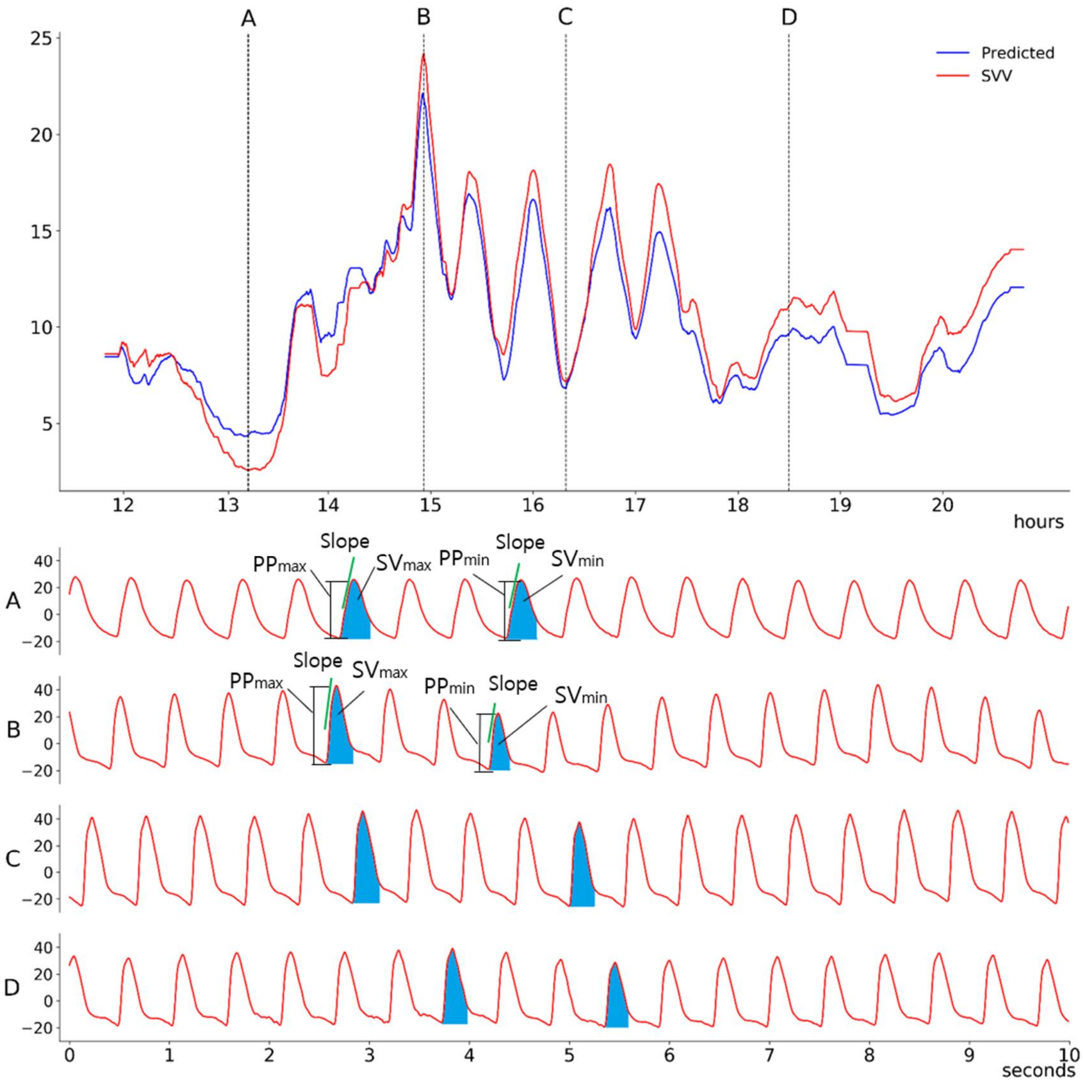

Figure 2. Representative plot of predicted SVV using the proposed deep learning model compared by SVV of FloTrac and Arterial blood pressure waveform (ABP). The model shows the competitive result of estimated SVV. A and C were slightly different variations and areas the lower SVVs of arterial blood pressure. B and D represent high SVV of large ABP variance and area differences.

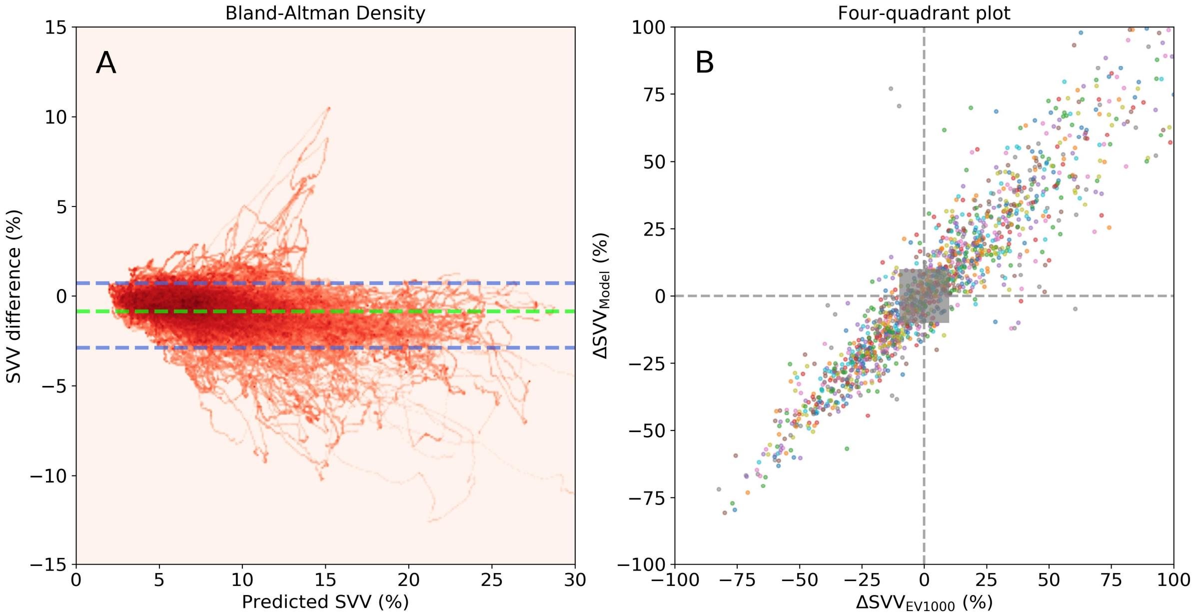

Figure 3. Bland Altman plot (A) and Four-quadrant (B) plot analysis between SVV of FloTrac and SVV of the proposed model. Each color represents patients. A central red zone is excluded.

Table 4. Trend Analysis of various pre-processing methods.

Data type	**Linear regression analysis**	**Bland-Altman analysis**		**Mean Absolute Error**	**Mean Squared Error**	**Concordance Rate (%)**
	Pearson correlation, *r* (95% CI)	Bias	95% Limits of agreement			
ABP signal	*0.91*	-1.00	-4.47 ~ 2.48	1.55	4.74	95.89%
Preprocessed ABP	*0.93*	-0.87	-4.34 ~ 2.59	1.30	4.08	96.23%
Frequency of ABP	*0.88*	-0.88	-5.03 ~ 3.27	1.52	5.08	94.85%
Slope of ABP	*0.93*	-1.00	-4.62 ~ 2.61	1.38	4.59	96.06%
Combined preprocessed and slope ABP	*0.94*	-0.93	-4.02 ~ 2.17	1.24	3.18	95.04%
All combined ABP	*0.95*	-0.85	-2.88 ~ 0.71	1.01	2.13	95.90%

Based on pre-processed data, the results are compared with the stroke volume variation (SVV) of the model and the SVV of the FloTrac. Preprocessed arterial blood pressure (ABP) waveform removed DC offset to remove baseline. Frequency data are the values that convert ABP to 1 ~ 12.2Hz using Fast Fourier Transform (FFT). The slope data are obtained by differential ABP waveform.

DISCUSSION

In this study, we predicted stroke volume variation using arterial blood pressure in general anesthesia operation. The proposed CNN model estimated SVV and accuracy that could replace the SVV of FloTrac. However, our model has yet to be tested in real-time general anesthesia surgery.

The proposed CNN model can solve the limitations of equipment including FloTrac. This model can obtain SVV values by solving a spatial problem and connecting it to the device anywhere when obtained ABP waveform. If an emergency occurs outdoors, or an operating room without a FloTrac, it can be administered without equipment, judging that there is not enough fluid. it can also save costs. In the case of FloTrac, the equipment itself is very expensive, and patients must purchase disposable medical supplies products at one use. However, measuring with the deep learning model does not cost money. With these deep learning model-based measurements, many patients who do not have SVV-based fluid management will be able to receive anesthesia management without any burden.

Many signal analysis deep learning model uses RNN models, which did not perform well and took a very long time when trying with LSTM on a sample dataset. We also tested the RCNN model, the RNN + CNN model, but it didn't perform well. The best performance was the repeated model of CNN strides that could not be dimension reduction.

In a typical CNN model, normalization is performed by applying the min-max method to input data and then deep learning is learned. However, in the ABP waveform, min-max normalization can lead to loss of information. The SVV predicted by the ABP waveform is known to make SVV measurements based on shape and slope. The FloTrac model, predicted by the ABP waveform, is known to measure SVV based on shape and slope. Therefore, the DC offset of the signal was removed without min-max normalization applied. Also, it is typical to apply max pooling to CNN, which is a problem with the ABP waveform. In the medical images used, high values often have information, but in ABP signals, there is often information even at low or medium values. So we applied a convolutional strides layer to learn dimension reduction. This process has improved performance over the previous model.

Deep learning models have different results depending on input data processing. The default ABP waveform shows low statistical results and improves with data preprocessing for each method. Removing the DC offset and slope of the data results in improved results. Frequency data shows rather low statistic results. The model is constructed by combining pre-processed data in several methods, and results are improved as input data increases to multiple channel models. This explains the effectiveness of verification to reduce overfit each other, rather than adding information. The correct SVV value of the equipment is a completely unmatched ABP waveform. Therefore, severe over-fitting occurs with just one signal. Thus, as channels are added, the results are improved.

Limitation

Since the model was trained with the SVV of the FloTrac, it is not possible to derive the correct value when there is a problem with the ABP signal. However, SVV has been steadily shown to be trusted parameter of fluid reactivity in adults [31], there will be no major problems with the model. We plan to use more accurate values such as echocardiogram to predict SVV in the future. In the future we will overcome the limitations of the current model.

Conclusion

We have shown that we can predict SVV using deep learning model. SVV could be measured with only ABP waveform without existing equipment. Besides, data processing and model improvement using patient vital signals from anesthesiologists will help other researchers. We would like to help patients who measure ABP waveforms but cannot measure SVV due to space and cost to get more help in accurate anesthesia quality management.

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ABSTRACT

BACKGROUND Stroke volume variation (SVV) was used as a predictor of fluid reactivity for patients with mechanical ventilation. However, measuring devices currently in use have limitations in terms of space and cost. SVV is not being measured in all patients with arterial blood pressure (ABP). The purpose of this study was to predict SVV with ABP waveform using a machine learning method and overcome limitations of current equipment.

METHODS Learning model using ABP waveforms and SVV acquired by Bx50, FloTrac. For model learning and examinations, patients were divided into three groups according to period and proportion. Training (n = 210, data = 3,620,386) validation (n = 217, data = 3,944,244), and test (n = 130, data = 947,954) set totally 557 patients and 8,512,564 data set of SVV. As one of the deep learning models, this study used a model of convolutional neural network (CNN). It applied preprocessing, multichannel, and dimension reduction to improve CNN model.

RESULTS Estimated SVV of the model and SVV of FloTrac were compared statistically. The model was improved using preprocessing and dimension reduction of ABP waveform in the samples. The model with min-max preprocessing and max-pooling for dimension reduction to have low correlation and high mean squared error (r=0.66, MSE = 22.86). The proposed model showed better results removing direct current (DC) offset of ABP waveforms and using convolutional strides to dimension reduction (r=0.91, MSE=6.92). The results of the basic signal were relatively low (r = 0.91, MSE = 4.74). SVV with three channel inputs and improved deep learning model structure appears to have high correlation (r=0.95), lower mean squared error (2.13), the high concordance rate of trend analysis (95.9%).

CONCLUSION We calculated SVV using a convolutional neural network (CNN) model. This model has a smaller error and similar performance compared by SVV of FloTrac. The CNN model can overcome space and cost problems limitations of FloTrac. The CNN model seems to be replaceable when the FloTrac device is not available.