Research Article

Fully Convolutional Neural Network Deep Learning Model Fully in Patients with Type 2 Diabetes Complicated with Peripheral Neuropathy by High-Frequency Ultrasound Image

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This study was aimed at exploring the diagnostic value of high-frequency ultrasound imaging based on a fully convolutional neural network (FCN) for peripheral neuropathy in patients with type 2 diabetes (T2D). A total of 70 patients with T2D mellitus were selected and divided into a lesion group (n=31) and a nonlesion group (n=39) according to the type of peripheral neuropathy. In addition, 30 healthy people were used as controls. Hypervoxel-based and FCN-based high-frequency ultrasound images were used to examine the three groups of patients to evaluate their diagnostic performance and to compare the changes of peripheral nerves and ultrasound characteristics. The results showed that the Dice coefficient (92.7) and mean intersection over union (mIOU) (82.6) of the proposed algorithm after image segmentation were the largest, and the Hausdorff distance (7.6) and absolute volume difference (AVD) (8.9) were the smallest. The high-frequency ultrasound based on the segmentation algorithm showed higher diagnostic accuracy (94.0% vs. 86.0%), sensitivity (87.1% vs. 67.7%), specificity (97.1% vs. 94.2%), positive predictive value (93.1% vs. 86.7%), and negative predictive value (94.4% vs. 84.0%) (P<0.05). There were significant differences in the detection values of the three major nerve segments of the upper limbs in the control group, the lesion group, and the nonlesion group (P<0.05). Compared with the nonlesion group, the patients in the lesion group were more likely to have reduced nerve bundle echo, blurred reticular structure, thickened epineurium, and unclear borders of adjacent tissues (P<0.05). In summary, the high-frequency ultrasound processed by the algorithm proposed in this study showed a high diagnostic value for peripheral neuropathy in T2D patients, and high-frequency ultrasound can be used to evaluate the morphological changes of peripheral nerves in T2D patients.

1. Introduction

Diabetes with peripheral neuropathy (PN) is one of the common chronic complications of diabetes [1]. The cause is that long-term high blood sugar causes continuous damage to peripheral nerves, which makes the peripheral nerves feel abnormal. Generally, it mainly damages the sense of temperature and pain, and the damage to the motor nerves is mild. Diabetes with PN, together with diabetic nephropathy and diabetic retinopathy, constitute the diabetic triad [2, 3]. The main clinical manifestations of the patient are the symmetry of the distal peripheral skin with coldness, tingling itching, and ant-walking sensation; sensory motivation disorders will also appear on the tip of the tongue; and the patient may also fall easily [4]. Type 2 diabetes (T2D) combined with PN (T2DPN) is generally seen in patients with a history of diabetes for more than 5 years, and patients with poor blood sugar control usually have PN [5–7]. The first clinical manifestation
is abnormal sensation, which mainly manifests as numbness in
doing the hands and feet, abnormal sensation, such as acupuncture-
like sensation, ant-walking sensation, itching sensation, or
hyperalgiesia [8]. This numbness is generally symmetrical, start-
ing from the distal end, and it is more common in the part of
wearing socks or wearing gloves, so it is also called gloves or
socks-like paresthesia in clinical practice [9]. In some patients,
the muscles of both lower limbs are atrophy, especially the mus-
cle atrophy between the tendons of the feet is more obvious [10].

For patients with T2D, early diagnosis and timely treat-
ment are the basic measures to prevent diabetic neuropathy.
At present, there are many ways to clinically check diabetic
PN, such as nerve conduction velocity test and quantitative
sensory test. However, these two tests all required specialist
operations and are time-consuming, laborious, and costly, so
it is limited in large-scale screening and routine examinations
in diabetes clinics [11–13]. Clinical studies have shown that
high-frequency ultrasound can clearly display the condition of
peripheral nerves and accurately provide information on the
course, distribution, echo, and anatomical relationship of
surrounding tissues [14]. In recent years, high-frequency ultra-
sound has been widely used in the display of normal neural
structures, the diagnosis of neuropathy, and the identification
of tumors inside and outside the nerves [15, 16]. However,
there are few studies on its diagnostic value in T2D mellitus
of tumors inside and outside the nerves [15, 16]. However,
the course of the disease shorter than 10 years (14 were males
and 17 were females), 39 cases with the course of the disease longer
than 10 years (18 were males and 21 were females). Patients
were divided into a lesion group (n = 31) and a nonlesion
group (n = 39) according to whether they had peripheral neu-
ropathy or not. In addition, 30 healthy subjects during the
same period were selected as the control group, including 14
males and 16 females. High-frequency ultrasound images
based on supervoxel and FCN were used to examine the three
groups of patients to evaluate their diagnostic performance
and to compare and analyze the changes of peripheral nerves
and ultrasound characteristics. The informed consent of all
patients was obtained, and this study had been approved by
the medical ethics committee of hospital.

Inclusion criteria are as follows: patients who met the diag-
nostic criteria with reference to the relevant diagnostic criteria
of T2DPN in the diagnostic criteria of diabetes, patients who
were confirmed with T2D through various biochemical tests,
patients with complete clinical data, and patients whose family
members know and sign the informed consent

Exclusion criteria are as follows: patients with a history of
relevant surgery; patients with other types of diabetes;
patients with a history of malignancy; those with other seri-
ous diseases; those with immune system disorders; patients
with allergies; those with poor adherence to the study;
patients with a history of hypertension, coronary heart dis-
ease (CHD), and neuropathy; and patients with no positive
signs on neurological examination.

2.2. Methods

2.2.1. Construction of FCN. FCN implements pixel-level classi-
fication, which is mainly based on the traditional convolu-
tional neural network model (CNN) with the following
adjustments. Firstly, the convolutional layer was used to
replace the fully connected layer in the traditional CNN
model. This effectively relieved the display of the input image
size by the fully connected layer and realized the simultaneous
prediction of multiple pixels, which effectively reduced the
computational complexity of the model. Secondly, the upsam-
ping process had been added. This guaranteed the size of the
output image. Thirdly, a cross-layer connection structure was
used, which solved rough segmentation caused by deconvolu-
tion. The basic structure of the FCN model and the CNN
model was shown in Figure 1.

In this study, an end-to-end CNN model fusion 3D
supervoxel method was proposed for image segmentation.
The basic structure of the model was shown in Figure 2.

The FCN model in this image was mainly composed of
convolutional layer, BN layer, and ReLU. The pooling win-
dow size of the pooling layer was 3 × 3, the step size was
set to 2, and the loss function used by the softmax layer as
shown in the following equation:

\[
\text{Loss} = - \sum_{i} \hat{u}_{n} \log f(z_{i}).
\]  

In the above equation, \( \hat{u} \) was the label value, and \( f(z_{i}) \)
referred to the probability that the sample belongs to different categories.

In this study, the SLIC supervoxel algorithm was adopted for image segmentation. It was assumed that the spatial position of a pixel in the five-dimensional space was \((a_i, b_j, c_i, d_j, e_j)\), and the position of the sample in the LAB color space was expressed as \((a_i, b_j, c_i)\); then, the position of the cluster center can be expressed as \((a_j, b_j, c_j)\).

At this time, the color distance from the \(i\)th pixel to the \(j\)th cluster center was expressed as below equation:

\[
D_{abc} = \sqrt{(a_j - a_i)^2 + (b_j - b_i)^2 + (c_j - c_i)^2}. \tag{2}
\]

The spatial distance from the \(i\)th pixel to the \(j\)th cluster center was given as follows:

\[
D_{de} = \sqrt{(d_j - d_i)^2 + (e_j - e_i)^2}. \tag{3}
\]

The color distance and the space distance were normalized, and the calculation equation after processing was as follows:

\[
D^* = \sqrt{\left( \frac{D_{abc}}{Lc} \right)^2 + \left( \frac{D_{de}}{Ls} \right)^2}. \tag{4}
\]

In the above equation (4), \(Lc = m\) and \(Ls = \sqrt{L/k}\).

2.2.2. HFUS Examination. The subjects all were performed with HFUS examination based on FCNN-DL model. After 15 minutes in a quiet state, the color ultrasound diagnostic apparatus was applied for examination. The frequency of the probe was 8-10 MHz. The specific inspection method was as follows. The patient was assisted to choose the prone position with fully exposed legs. The examination was started from the thigh base downwards the ankle; the cross-section was scanned firstly, and then, the probe was rotated 90 degrees to scan the longitudinal section to show the main nerves of the lower limbs, including sciatic nerve, common peroneal nerve, tibial nerve, common peroneal nerve, and tibial nerve.

2.2.3. Image Processing. The image data were normalized. The methods commonly used for data normalization processing included Min-Max and Z-score normalization. In this study, the Min-Max normalization method was used to normalize high-frequency ultrasound images. The calculation equation of this method was as follows:

\[
x^* = \frac{(x - x_{\text{min}})}{(x_{\text{max}} - x_{\text{min}})}. \tag{5}
\]

In the above equation, \(x^*\) was the normalized data, \(x_{\text{min}}\) was the minimum value in the pixel set, and \(x_{\text{max}}\) referred to the maximum value in the pixel set.

2.2.4. Evaluation Indicators. In this study, the indicators Dice similarity, mean intersection over union (mIOU), Hausdorff distance, and absolute volume difference (AVD) were adopted.
to compare the effects of algorithms in processing image data. The calculation equations for different indicators were given as follows:

$$\text{Dice} = \frac{2 \times TP}{(TP + FN) + (TP + FP)},$$  \hspace{1cm} \text{(6)}$$

In the above equations, TP was true positive, FP referred to false positive, TN was true negative, and FN represented false negative.

$$\text{mIOU} = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{TP}{TP + FN + FP} \right)_i,$$  \hspace{1cm} \text{(7)}$$

In the above equation (7), IOU was within 0 ~ 1, and n was the number of classification.

$$\text{Hausdorff} = \max \left[ \max_{a \in S} \min_{b \in \text{SEG_GT}} ||a - b||, \max_{b \in \text{SEG_GT}} \min_{a \in S} ||a - b|| \right].$$  \hspace{1cm} \text{(8)}$$

Hausdorff distance was used to measure the maximum distance of the surface in space. The smaller the value, the better the segmentation effect.

$$\text{AVD} = \frac{|V_S - V_{GT}|}{V_{GT}}.$$  \hspace{1cm} \text{(9)}$$

In the above equation (9), $V_S$ was the divided volume, and $V_{GT}$ referred to the real volume.

2.3. Statistical Analysis. The collected data were sorted, summarized, and analyzed by SPSS 23.0. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), single sample data was tested using the $t$-test; count data was tested by $\chi^2$ and expressed in the form of number of cases (%). $P < 0.05$ indicated that the difference was statistically significant.

3. Results

3.1. Segmentation Algorithm Test Results. To verify the effectiveness of the proposed algorithm for high-frequency ultrasound image segmentation, it was compared with Snake [19], CNN [20], FCN8s [21], and SegNet [22] for segmentation of high-frequency images of patients with diabetes and peripheral neuropathy. The segmentation effect was shown in Figure 3. It can be observed that the Snake, CNN, and FCN8s algorithms only obtained the approximate outline of the lesion but failed to capture the detailed features of the lesion in place. SegNet and the algorithm proposed could better segment and process the boundary details of the lesion, but the algorithm proposed in showed a better processing effect on the details of tissue texture and boundary.

Then, the evaluation indicators Dice, mIOU, Hausdorff, and AVD were adopted to quantitatively evaluate the segmentation effects of different algorithms, and the results were shown in Figure 4. It illustrated that the Dice and mIOU values after the Snake model divided the image were the smallest, while the Hausdorff and AVD values were the largest. On the contrary, the Dice and mIOU values of the proposed algorithm after image segmentation were the largest, while the Hausdorff and AVD values were the smallest.

3.2. Comparison of the Value of High-Frequency Ultrasound in Diagnosing Peripheral Neuropathy. 100 samples were included for diagnostic value analysis. Among them, 69 patients had no peripheral nerve disease (30 healthy people, 39 patients with type 2 diabetes) and 31 patients with peripheral neuropathy (type 2 diabetes with peripheral neuropathy). The conventional high-frequency ultrasound and algorithm processing were adopted to compare the value of high-frequency ultrasound for disease diagnosis. Routine ultrasound diagnosed 21 true positive cases, 65 true negative cases, 4 false positive cases, and 10 false negative cases. Algorithm-based high-frequency ultrasound diagnosed 27 true positive cases, 67 true negative cases, 2 false positive cases, and 4 false negative cases. The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of different methods were calculated, and the comparison of the diagnostic effects between the two groups of patients was shown in Figure 5. As it revealed, the value of algorithm-based high-frequency ultrasound diagnosis was significantly better than that of conventional ultrasound.

3.3. Comparison of Basic Patient Information. According to the diagnosis of high-frequency ultrasound and other data, among the 70 patients with type 2 diabetes, 31 had peripheral neuropathy, and 39 had no pathological changes. Therefore, the differences in the basic data of patients in the control group, the lesion group, and the nonlesion group were compared, and the results were shown in Table 1. There was no significant difference in the gender ratio and age of patients in three groups ($P > 0.05$). There was no significant difference in the course of disease data of patients between the lesion group and the lesion group ($P > 0.05$).

3.4. Distribution of Nerve Changes in Patients with Type 2 Diabetes and Peripheral Neuropathy. The nerve changes of patients with type 2 diabetes and peripheral neuropathy were
compared. As given in Figure 6, the proportion of patients with thickening of the sciatic nerve was the largest (76%), followed by the thickening of the common peroneal nerve (21%), and the proportion of patients with the tibial nerve damage was the lowest (3%).

3.5. Comparison of Nerve Changes in each Group of Patients. The length (D1), width (D2), and cross-section area (CSA) of the cubital fossa (MN), the radial nerve running along the nerve groove (RN), and between the inner epicondyle and the olecranon (UN) of the patient were measured and calculated, and the results were given in Table 2. It can be observed that there were significant differences in MN-CSA, RN-D1, RN-CSA, UN-D1, and UN-CSA in the control group, the lesion group, and the nonlesion group, and the differences were statistically significant (P < 0.05).

3.6. Comparison of Ultrasound Features in Patients with Type 2 Diabetes. The changes in ultrasound characteristics of patients with type 2 diabetes were compared in the lesion and nonlesion groups, and the results were shown in Figure 7. Compared with patients with type 2 diabetes with no peripheral neuropathy, patients with type 2 diabetes with peripheral neuropathy were more likely to have reduced nerve bundle echo, blurred reticular structure, thickened epineurium, and unclear borders of adjacent tissues. And the difference was statistically significant (P < 0.05).

4. Discussion

The incidence of diabetic PN is increasing year by year, and it can be as high as 50% in western countries. Its pathogenesis is not yet fully understood, and it may be related to the metabolic disorders and abnormal microcirculation of the body and the body’s own immune disorders [23–25]. Most of the disease has an insidious onset, and patients have no conscious symptoms at the beginning. When clinical symptoms appear, irreversible pathological changes have appeared in the peripheral
nerves, which increases the risk and difficulty of clinical treatment and prognosis [26]. Therefore, early diagnosis and discovery of peripheral nerve damage are subjects of close clinical attention [27].

Although the current clinical examination methods are relatively reliable and objective examination methods, they have the disadvantages of being time-consuming, laborious, and high cost, so they cannot be used in large-scale screening and diabetic outpatient examinations [28]. An ultrasound can measure the cross-sectional area of each nerve, which can provide a morphological basis for the evaluation of the degree of PN in diabetic patients, and it can also provide information on changes in nerve stiffness. In this study, HFUS was used to examine the neurological conditions of T2DPN patients, and the FCNN-DL model was adopted to improve the diagnostic accuracy of ultrasound examination and better explore the diagnostic efficiency of the examination. The results of this study showed that the use of FCN fusion supervoxel model for the processing of high-frequency ultrasound images of patients had better segmentation effect than Snake, CNN, FCN8s, and SegNet models. Villa et al. [29] pointed out that the FCN-based method was superior to other algorithms in the segmentation effect of ultrasound images. Jiang et al. [30] also proposed that the FCN algorithm had a significant segmentation effect on CT images. Wang et al. [31] and See et al. [32] pointed out that the supervoxel segmentation effect had better advantages in their research. The above results suggest that the supervoxel and FCN algorithms have good application prospects in medical image segmentation, and give certain support to the results obtained in this work.

Subsequently, this study compared the difference in the diagnostic value of high-frequency ultrasound in patients with peripheral neuropathy before and after the algorithm processing. The results showed that compared with conventional ultrasound, after high-frequency ultrasound imaging processed by the algorithm proposed in this study was used for the diagnosis of peripheral neuropathy in patients, the accuracy (94.0%), sensitivity (87.1%), specificity (97.1%), positive predictive value (93.1%), and negative predictive value (94.4%) were significantly improved. It suggests that the ultrasound image processed by the algorithm can improve the diagnosis effect of the disease [33].

High-frequency ultrasound imaging technology can clearly and intuitively display the nerve distribution and morphology of peripheral neuropathy in patients with type 2 diabetes, which provides very valuable information for the clinical diagnosis and treatment of the disease [14]. This study subsequently compared the changes in neuromorphology in patients with type 2 diabetes and peripheral neuropathy. The results showed that the patient’s elbow fossa’s inner and upper cross-sectional area, the long diameter and cross-sectional area of the radial nerve along the nerve groove, and the long diameter and cross-sectional area between the inner epicondyle and the olecranon of the elbow were significantly different. The above indicators of diseased patients were significantly greater than those of nonsurgery patients and healthy people. Such results are consistent with the findings of Liu et al. [34]. In addition, it was found in this study that patients with type 2 diabetes and peripheral neuropathy had a significantly increased probability of reduced nerve bundle echo, blurred reticular structure, thickened epineurium, and unclear borders of adjacent tissues. This may be used because the blood sugar level in the body is too high, which makes the peripheral nerve carbohydrate components accumulate too much, the internal osmotic pressure of nerve cells increases, and the cells develop edema, which in turn increases the volume of nerve fiber bundles [35].

5. Summary

According to the above analysis, it was concluded that high-frequency ultrasound processed by the FCN fusion algorithm based on hypervoxel had a high diagnostic value for peripheral neuropathy in patients with T2D; and high-frequency ultrasound can be used to assess morphological changes in peripheral nerves in patients with T2D. However, due to the loss of

| Item                  | Control group (n = 30) | Lesion group (n = 31) | Nonlesion group (n = 39) | F value | P value |
|-----------------------|------------------------|-----------------------|--------------------------|---------|---------|
| Gender (cases (%))    |                        |                       |                          |         |         |
| Males                 | 14 (46.7)              | 16 (51.6)             | 20 (51.3)                | 0.949   | 0.261   |
| Females               | 16 (53.3)              | 15 (48.4)             | 19 (48.7)                |         |         |
| Age (years old)       | 55.27 ± 2.8            | 57.62 ± 1.3           | 56.59 ± 1.4              | 1.337   | 0.148   |
| Course of disease (years) | —                     | 9.26 ± 1.3            | 9.58 ± 1.1               | 1.094   | 0.183   |

Figure 6: Changes of peripheral nerve.
Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors’ Contributions

Xiaoqiang Liu and Hongyan Zhou contributed equally to this work.

Table 2: Comparison of the measured values of the three major nerves of the upper limbs.

| Parameter | Lesion group (n = 31) | Nonlesion group (n = 39) | Control group (n = 30) | F value  | P value |
|-----------|----------------------|-------------------------|-----------------------|----------|---------|
| MN        |                      |                         |                       |          |         |
| D1        | 6.14 ± 0.32          | 5.63 ± 0.38             | 5.54 ± 0.45           | 2.096    | 0.094   |
| D2        | 2.89 ± 0.31          | 2.57 ± 0.22             | 2.46 ± 0.25           | 2.105    | 0.098   |
| CSA       | 13.89 ± 1.35         | 11.09 ± 1.21            | 10.76 ± 1.66          | 4.132    | 0.035*  |
| RN        |                      |                         |                       |          |         |
| D1        | 5.64 ± 0.45          | 4.81 ± 0.33             | 4.67 ± 0.49           | 3.769    | 0.041*  |
| D2        | 2.76 ± 0.34          | 2.34 ± 0.25             | 2.29 ± 0.34           | 1.577    | 0.116   |
| CSA       | 11.97 ± 1.75         | 9.07 ± 1.41             | 8.35 ± 1.55           | 5.549    | 0.009*  |
| UN        |                      |                         |                       |          |         |
| D1        | 5.11 ± 0.45          | 4.46 ± 0.36             | 4.29 ± 0.49           | 3.988    | 0.032*  |
| D2        | 2.74 ± 0.46          | 2.72 ± 0.25             | 2.73 ± 0.49           | 0.512    | 0.356   |
| CSA       | 10.98 ± 2.27         | 7.88 ± 1.09             | 7.75 ± 1.67           | 4.077    | 0.038*  |

Note: * the comparison was statistically significant (P < 0.05).

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