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Review article

A systematic review of generative AI approaches for medical image enhancement: Comparing GANs, transformers, and diffusion models

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ABSTRACT

Background: Medical imaging is a vital diagnostic tool that provides detailed insights into human anatomy but faces challenges affecting its accuracy and efficiency. Advanced generative AI models offer promising solutions. Unlike previous reviews with a narrow focus, a comprehensive evaluation across techniques and modalities is necessary.
Objective: This systematic review integrates the three state-of-the-art leading approaches, GANs, Diffusion Models, and Transformers, examining their applicability, methodologies, and clinical implications in improving medical image quality.
Methods: Using the PRISMA framework, 63 studies from 989 were selected via Google Scholar and PubMed, focusing on GANs, Transformers, and Diffusion Models. Articles from ACM, IEEE Xplore, and Springer were analyzed.
Results: Generative AI techniques show promise in improving image resolution, reducing noise, and enhancing fidelity. GANs generate high-quality images, Transformers utilize global context, and Diffusion Models are effective in denoising and reconstruction. Challenges include high computational costs, limited dataset diversity, and issues with generalizability, with a focus on quantitative metrics over clinical applicability.
Conclusion: This review highlights the transformative impact of GANs, Transformers, and Diffusion Models in advancing medical imaging. Future research must address computational and generalization challenges, emphasize open science, and validate these techniques in diverse clinical settings to unlock their full potential. These efforts could enhance diagnostic accuracy, lower costs, and improve patient outcome.

1. Introduction

Medical imaging is essential for diagnostics, employing modalities like MRI, PET-CT, and Ultrasound to analyze internal anatomy [48] and provide quantitative measurements. However, traditional imaging systems often produce low-resolution images impacted by noise and equipment limitations, which can hinder diagnostic accuracy and delay treatment. Enhancing image clarity is critical for timely and precise diagnoses, improving patient outcomes. Super-resolution (SR) techniques have emerged as a solution to improve image quality by transforming low-resolution images into high-resolution ones through hardware or software methods. Deep learning-based SR, driven by advancements in generative AI, has revolutionized medical image enhancement [77]. This paper examines three state-of-the-art generative AI approaches, namely, Generative Adversarial Networks (GANs), Transformers, and Diffusion Models for medical image enhancement. By conducting this study, valuable insights will be gained to answer these research questions:

RQ1: How have GANs, Transformers, and Diffusion Models been applied to different medical imaging modalities and enhancement tasks, and what are the key findings from existing research?

RQ2: What are the most commonly used evaluation metrics and datasets for assessing the performance of GANs, Transformers, and Diffusion Models in medical image enhancement?

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RQ3: What is the demonstrated clinical impact of these image enhancement techniques?
RQ4: Which approach provides the most promising overall results for medical image quality improvement?
RQ5: What are the primary challenges, limitations, and future opportunities in applying these generative AI approaches to medical image enhancement?

The paper is structured to comprehensively explore these questions. Section 2 details the methodology and research approach. Section 3 presents the three generative models approaches. Section 4 outlines the evaluation methodologies and used datasets. Section 5 provides the main results. Section 6 reviews the related works. Finally, Sections 7 and 8 summarize and discuss the main findings of this systematic review.

2. Methodology

2.1. Search strategy

The systematic review we present in this paper was conducted following the PRISMA methodology guidelines [59]. The databases used in this study were Google Scholar and PubMed. To facilitate our search, we were assisted by the Publish or Perish (PoP) application, which simplifies the process of finding relevant articles. The search was limited to publications in English between January 1st, 2022, and November 6th, 2024, during which 989 studies were found. To define the review's goal, keywords were carefully selected to obtain relevant articles. We designed our search query based on the terms "Medical Image Enhancement," "GAN", "Diffusion Models" and "Transformers"." The following search query was executed in PoP: ("Medical Image Enhancement" OR "Image Quality Improvement" OR "Super-Resolution") AND ("Generative Adversarial Networks" OR "GAN" OR "Transformers" OR "Diffusion Models") AND (MRI OR CT OR "X-ray" OR Ultrasound OR "Medical Imaging").

2.2. Study selection and data extraction

The search results were imported into the Rayyan web application [58] for duplicate removal and screening. To extract relevant articles for review, inclusion (IC) and exclusion (EC) criteria were applied, as follows:

Inclusion Criteria (IC):

- IC1: Studies focused on improving the quality of medical images.
- IC2: Studies testing enhancement techniques based on GANs, Transformers, or Diffusion Models.
- IC3: Studies comparing these approaches to each other or to other enhancement techniques.
- IC4: Studies addressing all medical imaging modalities.
- IC5: Articles published in English between 2022 and 2024.
- IC6: The study must be an original research article or a conference paper.

Exclusion Criteria (EC):

- EC1: Studies not focused on GANs, Transformers, or Diffusion Models.
- EC2: Studies addressing the enhancement of non-medical images.
- EC3: Studies not directly evaluating the quality of enhanced images.
- EC4: Studies using the three approaches for purposes other than improving the quality of medical images, such as segmentation, image synthesis, or any application not focused on enhancing image quality.
- EC5: Studies not written in English.
- EC6 Duplicated studies.

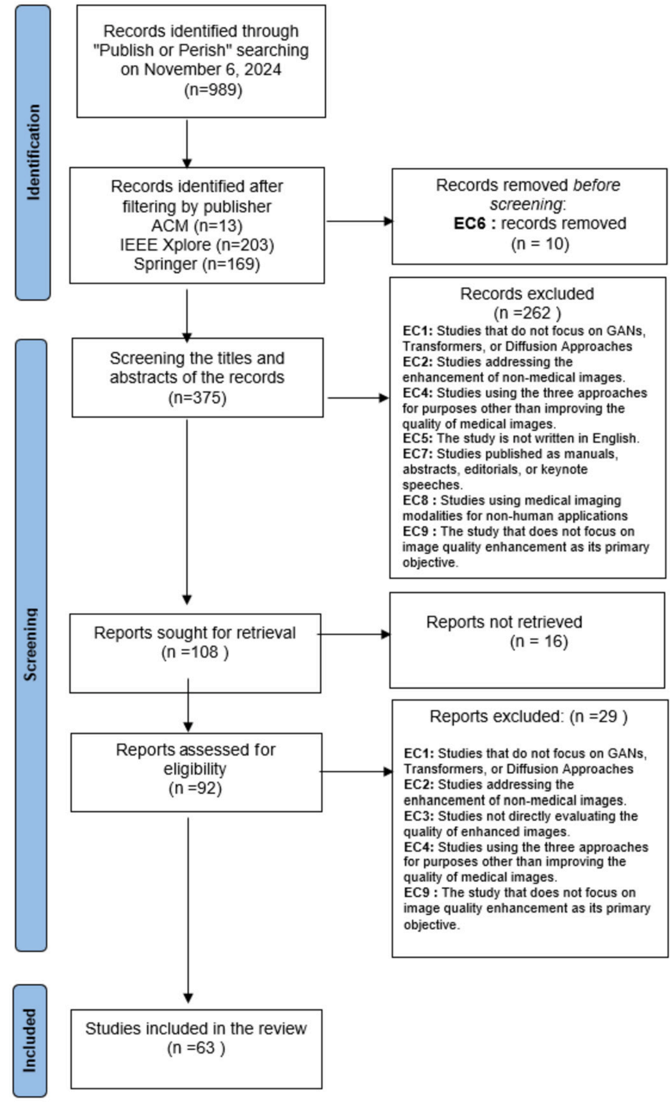

Fig. 1. PRISMA flow diagram describing the selection and screening process.

- EC7: Studies published as part of textbooks, abstracts, editorials, or keynote speeches.
- EC8: Studies using medical imaging modalities for non-human applications.
- EC9: Studies where enhancing image quality is not the primary objective, even if image enhancement is part of the process, such as when it is used as a preprocessing step for tasks like disease detection or diagnosis.

From 989 initial studies, 385 were selected by focusing on three reputable publishers: ACM, IEEE Xplore, and Springer, known for their high-quality, peer-reviewed articles and specialization in advanced technologies and medical research. After removing duplicates, 375 studies remained. The title and abstract of each were analyzed, and after applying the inclusion and exclusion criteria, 108 studies were retained. Of these, 92 provided access to their full text. After assessing the full texts for eligibility, 63 studies were included in this systematic review.

Tables 1, 2 and 3 present the list of articles classified per approach, while Fig. 1 provides a visual overview of the systematic review process, highlighting the key steps and decisions that led to the final selection of studies.

Table 1
List of included GANs studies.

Reference	Title	Reference	Title
Molahasani Majdabadi et al. [52]	Capsule GAN for prostate MRI super-resolution	Yin et al. [80]	Unpaired low-dose CT denoising via an improved cycle-consistent adversarial network with attention ensemble
Liu et al. [43]	Super-resolution reconstruction of CT images based on multi-scale information fused generative adversarial networks	Zhang et al. [86]	Contrastive adversarial learning for endomicroscopy imaging super-resolution
Nimitha and Ameer [56]	Multi image super resolution of MRI images using generative adversarial network	Zhong et al. [91]	Multi-Scale Attention Generative Adversarial Network for Medical Image Enhancement
Wicaksono et al. [78]	Super-resolution application of generative adversarial network on brain time-of-flight MR angiography: image quality and diagnostic utility evaluation	Reddy and Mohan [63]	Enhancing Medical Imaging: Noise Reduction and Super Resolution with Transfer Learning
Cao et al. [5]	Enhancing the MR neuroimaging by using the deep super-resolution reconstruction	Zhao et al. [90]	PCT-GAN: A Real CT Image Super-Resolution Model for Trabecular Bone Restoration
Zanzaney et al. [85]	Super Resolution in Medical Imaging	Nasser et al. [55]	Perceptual cGAN for MRI Super-resolution
Li et al. [37]	Multi-scale residual denoising GAN model for producing super-resolution CTA images	You et al. [81]	Fine perceptive GANs for brain MR image super-resolution in wavelet domain
Wang et al. [73]	A three-player GAN for super-resolution in magnetic resonance imaging	Balasubramanian et al. [4]	MRI super-resolution using generative adversarial network and discrete wavelet transform
Liu et al. [41]	Perception consistency ultrasound image super-resolution via self-supervised CycleGAN	Ankitha et al. [1]	Enhancing the resolution of Brain MRI images using Generative Adversarial Networks (GANs)
Reddy et al. [64]	Enhancing the Resolution of Chest X-ray Images with SRGAN and Sub-Pixel CNN	Zhou et al. [92]	Blind super-resolution of 3D MRI via unsupervised domain transformation
Dey et al. [12]	BliMSR: Blind Degradation Modeling for Generating High-Resolution Medical Images	Sun et al. [68]	Bidirectional Mapping Perception-enhanced Cycle-consistent Generative Adversarial Network for Super-resolution of Brain MRI images
Zhang et al. [87]	Motion artifact removal in coronary CT angiography based on generative adversarial networks	Lin et al. [40]	High-Resolution 3D MRI With Deep Generative Networks via Novel Slice-Profile Transformation Super-Resolution
Chen et al. [9]	Pathological image super-resolution using mix-attention generative adversarial network	Liu et al. [42]	R2D2-GAN: Robust Dual Discriminator Generative Adversarial Network for Microscopy Hyperspectral Image Super-Resolution
You et al. [82]	Brain MR images super-resolution with the consistent features	Madhav et al. [47]	Super Resolution of Medical Images Using SRGAN
Li et al. [36]	Fast and accurate super-resolution of MR images based on lightweight generative adversarial network	Han et al. [22]	A dual-encoder-single-decoder based low-dose CT denoising network
Huang et al. [27]	Edge-enhanced dual discriminator generative adversarial network for fast MRI with parallel imaging using multi-view information	Pan et al. [60]	Super-Resolution Reconstruction of Cell Images Based on Generative Adversarial Networks
Huang et al. [30]	Rethinking degradation: Radiograph super-resolution via AID-SRGAN	Li et al. [38]	Cross-Platform Super-Resolution for Human Coronary OCT Imaging Using Deep Learning
Khor et al. [33]	Ultrasound speckle reduction using wavelet-based generative adversarial network	Yetkin and Güveniş [79]	A Simulation Technical Feasibility Study for Removing Blur Artefacts from Emission Tomography Images Using Generative Adversarial Networks
Joshi et al. [32]	Enhancing Two dimensional magnetic resonance image using generative adversarial network	Geng and Zhou [17]	Image Super-Resolution Reconstruction of Pancreatic Carcinoma Based on Edge Repair Generative Adversarial Network
Komninos et al. [34]	Intra-operative OCT (iOCT) super resolution: A two-stage methodology leveraging high-quality pre-operative OCT scans	Dharejo et al. [13]	Multimodal-boost: Multimodal medical image super-resolution using multi-attention network with wavelet transform
Du and Tian [15]	Transformer and GAN-based super-resolution reconstruction network for medical images	Sedou Fofe et al. [66]	SIR-SRGAN-ResNeXt: A New Super-Resolution GAN with Self-Interpolation Ranker and ResNeXt Generator

Table 2
List of included Diffusion Models studies.

Reference	Title
Han and Huang [21]	Prostate MRI Super-Resolution using Discrete Residual Diffusion Model
Huang et al. [26]	MR Image Super-Resolution using Wavelet Diffusion for Predicting Alzheimer's Disease
Mao et al. [49]	DisC-Diff: Disentangled Conditional Diffusion Model for Multi-Contrast MRI Super-Resolution
Wang et al. [72]	InverseSR: 3D Brain MRI Super-Resolution Using a Latent Diffusion Model
Wang et al. [76]	Arbitrary Reduction of MRI Inter-slice Spacing Using Hierarchical Feature Conditional Diffusion
Mirza et al. [50]	Super Resolution MRI via Upscaling Diffusion Bridges
Cao et al. [6]	Accelerating multi-echo MRI in k-space with complex-valued diffusion probabilistic model
Chung et al. [10]	MR Image Denoising and Super-Resolution Using Regularized Reverse Diffusion
Gong et al. [18]	PET image denoising based on denoising diffusion probabilistic model

Table 3
List of included Transformers studies.

Reference	Title
Yu et al. [84]	RPLHR-CT dataset and transformer baseline for volumetric super-resolution from CT scans
Zhou et al. [93]	Deep-Learning Based Super-Resolution for Low-Dose CT
Güngör et al. [20]	TranSMS: Transformers for super-resolution calibration in magnetic particle imaging
Hu et al. [25]	Residual Dense Swin Transformer for Continuous Depth-Independent Ultrasound Imaging
Chen et al. [8]	LIT-Former: Linking in-plane and through-plane transformers for simultaneous CT image denoising and deblurring
Lyu et al. [45]	Multicontrast MRI super-resolution via transformer-empowered multiscale contextual matching and aggregation
Chen et al. [7]	Multi-Scale Style Aggregation Transformer-Based Network (MSAT-Net) for Multi-Contrast MRI Restoration: Super Resolution and Motion Artifact Reduction
Wang et al. [74]	Multi-contrast high quality MR image super-resolution with dual domain knowledge fusion
Huang et al. [28]	Accurate multi-contrast MRI super-resolution via a dual cross-attention transformer network
Forigua et al. [16]	SuperFormer: Volumetric transformer architectures for MRI super-resolution
Huang et al. [29]	TransMRSR: transformer-based self-distilled generative prior for brain MRI super-resolution

Table 4
Table of the Most Commonly Used Datasets in Medical Imaging Research.

Reference	Dataset	Description	Usage (%)
Organization [57]	IXI Dataset	Nearly 600 MRI scans from healthy subjects, including T1-, T2-, PD-weighted images, and more.	12.70%
Initiative [31]	ADNI	Alzheimer's neuroimaging dataset.	6.35%
Van Essen et al. [69]	HCP	High-resolution volumetric MRI data for neuroimaging research.	6.35%
Wang et al. [75]	NIH Chest X-rays	Over 112,000 Chest X-ray images from more than 30,000 unique patients.	4.76%
Health [23]	fastMRI	1,500 knee MRIs sampled on 3T and 1.5T systems.	7.94%
Conference [11]	MICCAI datasets	Medical imaging data for research and competitions.	1.59%
Rajpurkar et al. [62]	MURA	40,005 musculoskeletal radiographs of upper extremities.	1.59%
Armato III et al. [3]	LIDC-IDRI	Lung CT scans from the Lung Image Database Consortium.	1.59%
Archive [2]	TCIA datasets	Large cancer imaging database.	3.17%

3. Preliminaries - the deep learning approaches

3.1. Generative adversarial networks

Introduced by Goodfellow et al. [19], GANs consist of two competing neural networks: a generator that creates synthetic data and a discriminator that distinguishes real from fake. In medical imaging, GANs excel in image reconstruction and enhancement.

3.2. Diffusion models

Proposed by Sohl-Dickstein et al. [67], diffusion models learn data distributions through a forward process adding noise and a reverse process removing it. These models are promising for medical image reconstruction and enhancement.

3.3. Transformers

First introduced by Vaswani [70] for NLP, Transformers leverage a self-attention mechanism to capture global contextual relationships. Their success in computer vision has extended to medical imaging, where they address complex image analysis tasks by processing entire images simultaneously.

4. Evaluation methodology and datasets

This section addresses RQ2 by identifying commonly used evaluation metrics and datasets for assessing generative AI methods in medical image enhancement.

4.1. Overview of commonly used datasets in medical imaging research

A key challenge in medical imaging research is the limited availability of large, diverse datasets, which hinders the development of deep learning systems. Table 4 summarizes the open-source datasets identified in this study.

4.2. Image quality assessment metrics

Robust quality assessment is essential for validating medical image enhancement techniques, focusing on visual fidelity, structural preservation, and perceptual similarity:

- Full-reference Metrics: Compare enhanced images to reference images, providing detailed quantitative differences.
- No-reference Metrics: Assess quality without a reference, analyzing statistical and perceptual features.

4.2.1. Full-reference quality assessment metrics

PSNR: Peak Signal-to-Noise Ratio [89] measures pixel-level differences between original and enhanced images but struggles with capturing nuanced diagnostic details.

SSIM: Structural Similarity Index [61] evaluates image quality by analyzing brightness, contrast, and structure, aligning better with visual perception critical in medical diagnostics.

LPIPS: Learned Perceptual Image Patch Similarity metric, proposed by Zhang et al. [88], assesses differences in deep feature space, correlating well with human visual judgment.

FID: Frechet Inception Distance Heusel et al. [24] measures the distance between real and generated image distributions using feature representations from the Inception network.

4.2.2. Free-reference quality assessment metrics

NIQE: Natural Image Quality Evaluator [51] uses statistical features of image blocks and a Gaussian model to estimate image quality without a reference image.

PIQE: Perception-Based Image Quality Evaluator [71] divides images into blocks, detects local distortions, and aggregates block-level scores for overall quality assessment.

NRQM: No-Reference Quality Measure [46] predicts perceptual quality by combining local frequency, global frequency, and spatial features using regression forest modeling.

5. Result analysis

This section addresses RQ1, RQ3, RQ4, and RQ5 by analyzing the comparative performance of GANs, Transformers, and Diffusion Models across medical image enhancement tasks and modalities (RQ1), examining their clinical impact (RQ3), identifying the most promising approach for improving image quality (RQ4), and exploring challenges, limitations, and future opportunities in applying these generative AI methods (RQ5).

5.1. Applications of approaches by task and imaging modality

5.1.1. GAN-based approach

Magnetic Resonance Imaging (MRI): MRI imaging faces challenges like long scan times and limited resolution. GAN-based solutions improve resolution, reduce artifacts, and enhance diagnostic utility. For instance, CFGAN [82] excels in multi-scale reconstruction with high PSNR, SSIM, and FID performance, where You et al. [81] use a wavelet transformation-based GAN with texture-enhancing modules to improve structural similarity and detailed textures. Meanwhile, Joshi et al. [32] utilize a generator-discriminator framework to address hardware limitations and motion artifacts. Sun et al. [68] introduce a semi-supervised CycleGAN that utilizes perceptual loss and cycle-consistency loss to preserve texture details while training on unpaired data. SRGAN-based methods [81,4,1] integrate wavelet transformations and residual modules. Zanzaney et al. [85] add residual blocks and Parametric ReLU to enhance textures and high-frequency details. However, limitations persist: high computational demands [82], insufficient clinical validation [4], and performance variability across datasets [54].

Computed Tomography (CT): Low-dose CT imaging often produces noisy, lower-resolution images obscuring critical details. GANs have emerged as effective solutions, with models like PAUP-ESRGAN [43] using pyramidal attention to recover high-frequency details, MRDGAN [37] employing attention blocks and noise reduction to enhance microvascular details, and BliMSR [12] introducing Residual Multi-Head Attention for improved reconstruction. Other models like Improved CycleGAN [80], DESD-GAN [22], and TTSR [93] show improvements in visual quality and performance metrics. However, limitations persist: PAUP-ESRGAN [43] lacks clinical dataset validation, MRDGAN [37] and BliMSR [12] require further validation, and Improved CycleGAN [80] may generate artifacts. TTSR [93] has high-contrast artifacts, limiting clinical reliability. These challenges highlight the need for continued research and validation to improve GAN-based CT imaging methods.

Microscopy imaging: Microscopy imaging, including cellular, hyperspectral, and confocal methods, faces noise and equipment interference, affecting image quality. GANs show potential in addressing these issues. For instance, Light-ESRGAN [60] improves image details with a Convolutional Block Attention Module and a lightweight U-Net. R2D2-GAN [42] uses multi-scale fusion and dual discriminators to enhance hyperspectral image resolution. Other studies [65] apply convolutional layers and parametric ReLU for better resolution and edge recovery in microscopic images. GANs have improved resolution and visual quality without losing key details. However, limitations remain: Light-ESRGAN [60] struggles with generalizability across different cellular images and computational efficiency on resource-constrained platforms, and [65] requires further validation across modalities. Additionally, GANs' computationally intensive training limits practical applicability. MAGAN [91] faces issues with artifacts affecting the enhancement of unwanted features.

Other Imaging Modalities: Various imaging modalities, such as ultrasound, chest X-ray, OCT, emission tomography, and endomicroscopy, face challenges like noise, low resolution, and motion blur, hindering diagnostics. GANs offer promise solutions: self-supervised learning improves ultrasound super-resolution [41], wavelet transformations reduce speckle noise [33], SRGAN enhances chest X-ray resolution [64], CPSA-GAN boosts OCT resolution [38], ESRGAN mitigates emission tomography motion blur [79], and contrastive GANs refine endomicroscopy for biopsies [86]. Despite advancements, GANs face challenges in generalizability, high computational demands, and real-time application, requiring further research for reliable medical imaging enhancement.

5.1.2. Diffusion models-based approach

Magnetic Resonance Imaging (MRI): Diffusion models in magnetic resonance imaging (MRI) address key challenges like low spatial resolution, inter-slice spacing, and noise. Han and Huang [21] demonstrate how discrete residual diffusion overcomes issues like over-smoothing and mode-crashing in GAN-based methods, while Huang et al. [26] show the effectiveness of wavelet diffusion in enhancing structural details for Alzheimer's diagnosis. The work of Mao et al. [49] highlights multi-contrast MRI improvements through disentangled U-Net architecture with squeeze-and-excitation modules and curriculum learning, and Wang et al. [76] propose a hierarchical approach (HiFE) for generating high-fidelity in-between slices, boosting segmentation accuracy. Other innovations include the works of Mirza et al. [50] and Cao et al. [6] which combine forward and reverse diffusion processes for image upscaling and k-space acceleration, respectively, further underscoring their adaptability across tasks. Despite their strengths, diffusion models face limitations, including high computational demands [72,26] are constrained by its single-level wavelet transform framework, potentially limiting generalizability, slow sampling speeds [76], phase wrapping issues [6], and the need for accurate noise parameter estimation [10], requiring further optimization for clinical applicability.

Positron Emission Tomography (PET): Diffusion models in PET imaging tackle noise and uncertainty, aiding diagnosis and treatment. Gong et al. [18] introduce a Denoising Diffusion Probabilistic Model with a U-Net structure, leveraging MR priors for enhanced denoising and image fidelity. It surpasses traditional methods in accuracy, detail preservation, and provides uncertainty maps for diagnosis.

5.1.3. Transformer-based approach

Magnetic Resonance Imaging (MRI): Transformer-based models in MRI imaging address challenges like noise, artifacts, and multi-contrast imaging. Low-field MRI often suffers from these issues, while multi-contrast MRI requires effective data fusion. Huang et al. [28] use a dual cross-attention mechanism to tackle multi-contrast fusion, and Wang et al. [74] focus on preserving high-frequency details and improving data integration. Transformers enhance MRI tasks like super-resolution and artifact reduction, leveraging attention mechanisms for improved performance. For example, Lyu et al. [45] use a Swin-transformer-based module for better texture and boundary preservation, while Chen et al. [7] employ crossed-dual-transformer modules for super-resolution and motion artifact reduction. Forigua et al. [16] demonstrate the advantage of 3D relative positional encoding in volumetric MRI over 3D CNNs. Despite these advancements, challenges such as high computational costs, hardware constraints, as evidenced in [16,7], the need for 3D extension Huang et al. [28], as well as difficulties in generalizing across datasets, hinder clinical adoption. Continued optimization and validation are necessary to unlock the full potential of transformers in clinical MRI.

Other Imaging Modalities: Transformer-based models are advancing medical imaging, addressing challenges in CT, MPI, and ultrasound. In CT, Yu et al. [84] enhance volumetric super-resolution with transformers, tackling low resolution and high radiation exposure. In MPI, Güngör et al. [20] improve reconstruction quality with data-consistency modules to address low signal-to-noise ratios. Ultrasound benefits from Hu et al. [25], who mitigate depth-dependent resolution issues with noise suppression. Additionally, Chen et al. [8] use a dual-plane transformer to reduce noise and blur in CT images. Despite these advancements, challenges persist, such as high computational demands, dataset variability, and occasional artifacts. For instance, Yu et al. [84]'s model lacks clinical validation, and Güngör et al. [20] experiences performance degradation at higher super-resolution factors.

5.1.4. Combination-based approach

Combining transformers and GANs enhances medical imaging by uniting global context modeling with high-fidelity generation, addressing low-resolution MRI and low-dose CT challenges.

For instance, Huang et al. [29] use convolutional blocks for local processing and transformer blocks for long-range dependencies, enhanced by a pre-trained GAN and techniques like the StyleSwin decoder for high-quality reconstructions. Du and Tian [15] combine transformer layers for global context and GAN components for fine detail generation, outperforming traditional methods like EDSR [39] and WDSR [83] in super-resolution tasks. Despite their strengths, these hybrid models face challenges such as high computational demands and the need for large datasets for training [83]. Additionally, performance variability across datasets and the lack of clinical validation hinder their widespread adoption. Addressing these limitations is essential for improving efficiency and accessibility in medical imaging tasks.

5.2. Quantitative evaluation

In this section, we analyze the quantitative performance of the reviewed methods based on the PSNR and SSIM metrics. The results, categorized by the Transformer, Diffusion Models, and GANs approaches, are summarized in Table 5. Each table details the datasets, upscaling factors, and implementation setups.

The upscale factor refers to the ratio by which the resolution of a low-resolution image is increased to generate a higher-resolution version. It quantifies the degree of enlargement applied during the super-resolution process. This factor plays a crucial role in enhancing the resolution and revealing finer details in the upscaled image, allowing for more precise and clearer visual information.

Subsequently, we cover and highlight the following key findings:

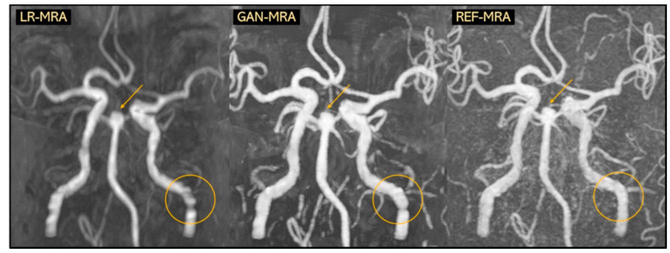

Fig. 2. A basilar tip aneurysm (arrow) was correctly identified by both raters on low-resolution MRA (left), GAN-reconstructed MRA (middle), and routine (high-resolution) MRA (right).

- Transformers:
  LIT-Former achieves the highest PSNR (43.10 dB) on clinical datasets, and TransMRSR scores the highest SSIM (0.9843) on the IXI dataset with an upscale factor of $\times 4$. TranSMS shows the lowest PSNR (20.89 dB) with an upscale factor of $\times 8$ on the simulated dataset and DCAMSR scores the lowest SSIM (0.637) with an upscale factor of $\times 8$ on the fastMRI dataset.
- Diffusion Models:
  HiFi-Diff excels with the highest PSNR (39.50 dB) and SSIM (0.9890) on the HCP dataset with an upscale factor of $\times 4$. Conversely, WaveDif records the lowest PSNR (20.9527 dB) and SSIM (0.7563) on the ADNI dataset at high upscale factors.
- GANs:
  The highest PSNR (45.49 dB) is achieved on the FastMRI dataset with an upscale factor of $\times 2$, and SRGAN achieves the highest SSIM (0.996) on the Lung CT dataset. However, it is important to note that while GANs achieved the best scores, these exceptional results contrast with their typical performance, which tends to be highly sensitive to datasets and image modality variations. MAGAN and CPSA-GAN display poor performance with the lowest PSNR (15.31 dB) and SSIM (0.31), highlighting dataset sensitivity and reconstruction challenges.

5.3. Qualitative evaluation

Qualitative evaluation is essential for assessing the visual and diagnostic improvements achieved through advanced computational approaches in medical imaging. Two key studies involved expert radiologists to validate these methods, focusing on subjective image quality and diagnostic accuracy. In the study of Wicaksono et al. [78], radiologists evaluated the visibility of vessels in low-resolution MRA (LR-MRA), GAN-reconstructed MRA (GAN-MRA), and routine high-resolution MRA. As shown in Fig. 2, GAN-MRA significantly improved vessel visibility compared to LR-MRA, with higher mean scores for both proximal and distal vessels. For example, distal vessel visibility scored 4.18 $\pm$ 0.84 with GAN-MRA versus 2.53 $\pm$ 0.78 with LR-MRA. However, GAN-MRA remained inferior to routine MRA. Radiologists showed substantial agreement, with a weighted Cohen's kappa of 0.75 and an ICC of 0.86. Diagnostic tests confirmed that GAN-MRA reduced false negatives, especially for aneurysm detection. Another study of Zhang et al. [87] assessed GAN-generated CCTA images. Radiologists used a 5-point Likert scale to evaluate motion artifact reduction and overall image quality. GAN-generated images scored higher than motion-affected images, demonstrating significant artifact reduction and enhanced diagnostic utility. Robust interobserver agreement (ICC) further validated these findings, and diagnostic accuracy metrics showed that GAN-generated images performed comparably to reference images in detecting clinically significant stenosis. These studies underscore the importance of expert-driven qualitative assessments in validating image quality improvements and highlight the transformative role of deep learning models in advancing medical imaging.

Table 5
Synthesis of the studies.

Ref	Method Name	Datasets	upscale	PSNR (dB)	SSIM	Implementation Setup
Synthesis of Transformer-Based Studies						
Yu et al. [84]	TVSRN	RPLHR-CT	-	38.609 ± 1.721	0.936 ± 0.024	PyTorch, and trained on NVIDIA A6000 GPUs
Güngör et al. [20]	TranSMS	Simulated Dataset	×2	26.35	-	-
			×4	25.72	-	
			×8	20.89	-	
Hu et al. [25]	RDSTN	MICCAI USenhance carotid	× 1.6	40.16	-	-
			× 2	36.30	-	
Chen et al. [8]	LIT-Former	Simulated Dataset	-	34.35 ± 1.72	-	NVIDIA V100 GPUs
		Clinical Datasets	-	43.10 ± 1.25	-	
Lyu et al. [45]	McMRSR++	fastMRI	×2	37.36	0.9503	Pytorch on Tesla A100 GPUs (8×80 GB)
			×4	31.20	0.8779	
Zhou et al. [93]	TTSR	NIH	-	31.16 ± 1.38	0.73 ± 0.06	-
Wang et al. [74]	EMFU	IXI dataset	×2	38.34	0.984	Nvidia GEFORCE GTX 1080 Ti GPUs
			×4	34.22	0.974	
Forigua et al. [16]	SuperFormer	HCP	-	32,4742 ± 2,9847	0,9059 ± 0,0271	PyTorch and train the model on a workstation with 4 Nvidia RTX 8000 GPUs
Huang et al. [28]	DCAMSR	fastMRI	×4	32.20	0.721	Adam optimizer for 50 epochs with a batch size of 4 on 8 Nvidia P40 GPUs
			×8	30.97	0.637	
Huang et al. [29]	TransMRSR	IXI dataset	×4	37.37	0.9843	two NVIDIA Tesla V100 GPUs based on PyTorch framework
			×8	30.42	0.9443	
Synthesis of DM-Based Studies						
Han and Huang [21]	DR-DM	PROSTATEx dataset	×4	21.71	0.76	yTorch framework on an NVIDIA Tesla A100 GPU
Chung et al. [10]	-	fastMRI	-	30.46	0.846	-
Huang et al. [26]	WaveDif	ADNI	×2	28.8190	0.9226	Nvidia RTX 3090 GPUs
			×4	27.1522	0.8201	
			×8	20.9527	0.7563	
Mao et al. [49]	DisC-Dif	IXI dataset	×2	37.64	0.9873	two NVIDIA RTX A5000 24 GB GPUs
			×4	31.43	0.9551	
Wang et al. [76]	HiFi-Diff	HCP dataset	×4	39.50 ± 2.285	0.9890 ± 0.0040	NVIDIA A100 40G with PyTorch
			×6	37.41 ± 2.314	0.9827 ± 0.0054	
Mirza et al. [50]	SRDB	IXI dataset	×2	34.9 ± 1.9	-	nVidia RTX 4090 GPU via the PyTorch framework
			×4	28.8 ± 1.8	-	
Chung et al. [10]	-	fastMRI	-	30.46	0.846	2×RTX 2080Ti GPUs
Gong et al. [18]	DDPM-PET	FDG dataset	-	31.45 ± 0.9 dB	0.87 ± 0.0	-
Synthesis of GAN-Based Studies						
Dey et al. [12]	BliMSR	LIDC-IDRI	-	26.48864 ± 6.89493	0.90146 ± 0.04583	NVIDIA a100 GPU
Yin et al. [80]	improved CycleGAN	'Lung-PET-CT-Dx' and a real clinical dataset	-	30.150	0.914	PyTorch on a NVIDIA RTX 2070S GPU with Intel Core i7-9700 K
Zhao et al. [90]	PCT-GAN	custom Dataset	-	30.122	-	PyTorch on an NVIDIA PTX 2080 Ti GPU
Madhav et al. [47]	SRGAN	Lung CT	-	32.95	0.996	Google Colab
Han et al. [22]	DESDGAN	Mayo Dataset	-	31.6833 ± 1.9486	0.8952 ± 0.0387	NVIDIA GTX 2080 Ti GPU
Zhang et al. [86]	SCGAN	BreastCLE	-	40.878 ± 2.887	0.9742 ± 0.0140	Intel Core i9-7900X, NVIDIA 3090Ti GPUs
		CLE1000 Datasets	-	32.431 ± 2.326	0.9105 ± 0.0254	
Yetkin and Güveniş [79]	ESRGAN	SPECT Dataset	-	32.21	0.9411	AMD Ryzen 5 3600X, NVIDIA RTX 2070 GPU with 8GiB RAM
Komninos et al. [34]	-	Hospital Datasets	-	31.45 ± 0.9	0.82 ± 0.0	NVIDIA Quadro P6000 GPU with 24 GB memory
Zhong et al. [91]	MAGAN	CORN-2	-	15.31	0.793	Intel (R) Xeon (R) Gold 633, Nvidia Geforce RTX 3090
Reddy and Mohan [63]	-	STARE Retinal dataset	-	37.17	0.85	batch size of lOon a Google Colab GPU
Liu et al. [42]	R2D2-GAN	real dataset	×4	40.57 ± 0.15	0.94 ± 2e-4	NVIDIA GeForce RTX 3090 GPUs on PyTorch framework
			×8	38.96 ± 0.16	0.92 ± 2e-4	
			×16	36.51 ± 0.32	0.87 ± 4e-4	

(*continued on next page*)

Table 5 (*continued*)

Ref	Method Name	Datasets	upscale	PSNR (dB)	SSIM	Implementation Setup
Zhou et al. [92]	-	HCP	-	34.793 ± 2.246	0.919 ± 0.005	the implementation is based on TensorFlow
Lin et al. [40]	SPTSR	MRI Dataset	-	29.08 ± 2.92	0.92 ± 0.45	-
Nasser et al. [55]	SRResNet+PD+PL	Super MUDI	-	-	0.83	12GB GeForce RTX 2080 GPUs
Molahasani Majdabadi et al. [52]	-	PROSTATEx datasets	×4	21.09	0.74	Tesla V100 (16 GB)
			×8	19.77	0.60	
Nimitha and Ameer [56]	-	prostate cancer datasets	-	30.58 ± 0.76	0.8105 ± 0.0656	Google Colab Pro and NVIDIA DGX machine with GPU A100
Wang et al. [73]	-	Resolution dataset	-	36.922	0.953	NVIDIA's Ampere 100 GPU
Li et al. [36]	-	fastMRI	×2	45.49	0.9915	NVIDIA GeForce GTX 3080 GPU
			×4	34.48	0.9262	
Huang et al. [27]	PIDD-GAN	Calgary Campinas dataset	-	32.3694 ± 0.4443	0.9425 ± 0.0046	NVIDIA TITAN RTX GPU with 24GB GPU memory
You et al. [82]	CFGAN	ADNI	×2	29.91	0.9381	Pytorch on Nvidia Titan RTX
			×4	29.08	0.8562	
You et al. [81]	FP-GANs	ADNI	×4	28.30	0.8816	Pytorch on Nvidia Titan RTX
			×8	26.78	0.8456	
		MultiRes_7T Dataset	×4	27.60	0.9178	
			×8	21.30	0.8036	
Balasubramanian et al. [4]	Wavelet-based SRGAN	Custom dataset	-	29.44	0.92	-
Joshi et al. [32]	-	ADNI	-	26.403804	0.787986	PyTorch on NVIDIA V100
Sun et al. [68]	-	custom Dataset	-	29.41 ± 3.71	0.914 ± 0.048	PyTorch deep learning framework
Li et al. [38]	CPSA-GAN	custom Dataset	-	22.33	0.31	two RTX A6000 GPUs
Huang et al. [30]	AID-SRGAN	MURA-mini	×2	34.11	0.9590	batch size of 32 on two TITAN X (Pascal) GPUs
			×4	31.21	0.9506	
Geng and Zhou [17]	ERGAN	CPTAC-PDA	×4	30.95	0.9179	TensorFlow 2.0 on NVIDIA GeForceRTX3060 GPU
			×8	25.48	0.7475	
Liu et al. [43]	PAUP-ESRGAN	TCIA Abdomen Dataset	×2	30.717	0.942	Intel i7-12700F CPU, NVIDIA GeForce RTX3090.
			×4	29.219	0.934	
			×8	28.297	0.929	
Reddy et al. [64]	modified ESPCN	Chest X-ray	-	35.17	0.81	-
Pan et al. [60]	Light-ESRGAN	PMO	-	32.338	0.861	Intel(R)i7-12700F, NVIDIA GeForce RTX3060
Wicaksono et al. [78]	GAN-MRA	Custom dataset	-	23.3	0.66	Python 3.6 and Tensorflow 2.5 library on Windows 10
Khor et al. [33]	WGAN-DUS	Waterloo-I Dataset	-	31.21	0.932	-
Li et al. [37]	MRDGAN	Custom dataset	-	35.89	0.953	Adam optimizer with the batch size of 12
Zhang et al. [87]	-	Custom dataset	-	26.1(24.4–27.5)	0.860 (0.830–0.882)	two graphic processors (Titan RTX, Nvidia) with 48 GB of graphics memory
Liu et al. [41]	-	CCA-US	-	35.222	0.919	Adam optimizer, starting with a learning rate of 0.001
		US-CASE	-	32.491	0.876	
Chen et al. [9]	MASRGAN	PathImgSR dataset	-	25.33	0.6730	Nvidia TITAN Xp GPU using the PyTorch framework
Sedou Fofe et al. [66]	SIR-SRGAN-ResNeXt	Breakhis-400x dataset	-	37.2361	0.9891	NVidia A100SXM4 GPU and 32GB of memory
		Messidor-2 dataset	-	42.079	0.9827	
Du and Tian [15]	T-GAN	knee MRI	-	34.92	0.9496	-
		abdominal MRI	-	34.69	0.9353	

5.4. Challenges and perspectives

Despite their remarkable progress in medical imaging, GANs, Transformers, and Diffusion Models face several overarching challenges and hold promising perspectives for future development. One significant challenge lies in achieving generalization across various imaging modalities and datasets, which is crucial for ensuring that these models can be broadly applicable in diverse clinical settings. Additionally, the high computational cost and complexity associated with these advanced models remain hurdles, particularly in resource-constrained environments. Noise and artifacts in reconstructed images also continue to pose challenges, as they can impact diagnostic accuracy and limit clinical utility. The scarcity of large, diverse, and annotated datasets further complicates model training, making it difficult to achieve robust performance across different imaging scenarios. On the other hand, the potential for growth in these technologies is immense. Expanding their application to include a broader range of imaging modalities, such as CT, ultrasound, and 3D MRI, could significantly enhance their clinical relevance. Additionally, future research should focus on optimizing computational efficiency, enabling real-time processing and deployment in clinical workflows. Validation in diverse clinical settings, alongside evaluations conducted by medical professionals, is crucial to bridge the gap between technical advancements and real-world impact. By addressing these challenges and pursuing these perspectives, GANs, Transformers, and Diffusion Models have the potential to revolutionize medical imaging and provide more accurate, accessible, and efficient diagnostic tools.

6. Related literature review work

Previous studies have thoroughly explored several image resolution enhancement techniques, focusing on advanced methods like Convolutional Neural Networks (CNNs), Diffusion Models, GANs, and deep learning for CT image improvement. Dixit and Yadav [14] reviewed modern CNN architectures used in super-resolution, particularly models like ESRGAN, which perform well at high upscaling factors. Their analysis emphasized the importance of perceptual loss functions and reference-less evaluation methods, especially in unsupervised models. Moser et al. [53] focused on diffusion models, which have made significant strides in producing more realistic and aesthetically pleasing super-resolved images compared to traditional techniques. Li et al. [35] presented a detailed survey of deep learning techniques applied to CT image improvement. They reviewed algorithms addressing denoising, super-resolution, and metal artifact correction, underscoring deep learning's impact on enhancing CT image clarity and diagnostic utility. Liu et al. [44] provided an extensive overview of GANs, which have shown great potential for image restoration and enhancement tasks, including super-resolution. These studies collectively highlight the evolving nature of image super-resolution methods, outlining each technique's strengths and limitations while offering insights into ongoing challenges. Our review integrates GANs, Diffusion Models, and Transformers, comparing their effectiveness in improving medical image quality. Unlike previous reviews that focused on individual techniques, this review offers a cross-modal comparison of these methods across various medical imaging tasks. By evaluating different variants within each approach, this paper provides new insights into their potential and challenges in real-world medical applications.

7. Discussion

This systematic review highlights the contributions of GANs, Transformers, and Diffusion Models in addressing key challenges in medical imaging, such as low resolution, noise, and structural limitations that impact diagnostic accuracy. These approaches have proven effective in improving image clarity and quality across various modalities.

GANs excel at generating high-quality images through adversarial training, Transformers leverage global contextual information for image analysis, and Diffusion Models show promise in denoising and reconstruction. However, these techniques have limitations: GANs can be unstable and introduce artifacts, Transformers are computationally demanding, and Diffusion Models involve slower processing and high resource consumption.

While most studies focus on quantitative metrics to evaluate improvements in image quality, these assessments fall short of achieving the ultimate goal: clinical validation. The transition to real-world clinical settings requires rigorous testing to ensure reliability in diagnosis and treatment. Issues such as the need for models that generalize across diverse datasets, high computational costs, and limited annotated datasets. Moreover, among the 63 analyzed studies, only 12 provided access to their code. This lack of availability hinders reproducibility and slows the pace of research. Promoting open science practices could accelerate innovation and collaboration in the field.

While challenges persist, the potential of these techniques to enhance diagnostic accuracy, reduce costs, and improve patient outcomes is clear. Future research should focus on optimizing computational efficiency, enhancing model generalizability, and prioritizing validation in clinical environments. A collaborative approach will help bridge the gap between technical innovation and practical clinical application, advancing medical imaging.

8. Conclusion

Medical imaging plays a vital role in diagnostics but often faces challenges such as low resolution, noise, and structural limitations that compromise image quality and accuracy. This systematic review has provided a comprehensive evaluation of the application of advanced generative AI techniques, specifically Transformers, GANs, and Diffusion Models, for medical image enhancement, focusing on their capabilities, limitations, and future potential. While the field has seen remarkable progress, particularly in improving image clarity and diagnostic utility, the journey toward integrating these techniques into everyday clinical practice continues. For future work, key areas include enhancing model generalizability across various imaging modalities and datasets, reducing computational complexity, and prioritizing robust validation in clinical environments. Addressing these challenges will be critical to unlocking the full potential of generative AI in medical imaging. By leveraging the strengths of these approaches and fostering a collaborative research ecosystem, the medical imaging community can accelerate innovation, ultimately contributing to improved patient care and outcomes.

Summary table

What was already known on the topic?

- Generative AI models have shown significant potential in enhancing medical image quality.
- Previous reviews have largely focused on individual techniques and their applications in tasks like image resolution enhancement and noise reduction.

What this study adds to our knowledge?

- Offers a comprehensive comparison of three leading generative AI approaches: GANs, Diffusion Models, and Transformers, evaluating their performance across various imaging modalities and tasks while highlighting their unique strengths and limitations.
- Identifies that GANs excel in producing high-quality images via adversarial training, Transformers effectively leverage global contextual information for image analysis, and Diffusion Models demonstrate promise in noise reduction and image reconstruction through iterative processes.
- Highlights critical gaps in the field, such as the lack of clinical validation, overreliance on quantitative metrics, and the need for

diverse, well-annotated datasets to ensure generalizability across different imaging modalities.
- Stresses the need to address computational challenges, enhance dataset diversity, and adopt open science practices to drive advancements and facilitate the clinical adoption of these technologies.

CRediT authorship contribution statement

Chaimaa Oulmalme: Writing – original draft, Methodology, Investigation, Data curation, Conceptualization. **Haïfa Nakouri:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Funding acquisition, Conceptualization. **Fehmi Jaafar:** Writing – review & editing, Validation, Supervision, Project administration, Funding acquisition.

Ethics

This systematic review does not involve human participants, and all data analyzed in this study were publicly available.

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Declaration of competing interest

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