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REAL-TIME MULTIMODAL PROGNOSIS IN LIVER TRANSPLANTATION USING AN ITERATIVE CROSS-ATTENTION FUSION NETWORK

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ABSTRACT

The correct and timely diagnosis following liver transplantation depends on the collation of disparate clinical, radiologic and microscopic data. In this paper, we present the Iterative Cross-Attention Fusion Network (ICAF-Net), a multimodal deep-learning based approach to address three key challenges for graft survival prediction, post-transplant complication detection, and readmission risk assessment. It consists of five components: Spatio-Temporal Cross-Modality Attribution Encoder (STCMAE), Radiopathological Graph Attention Alignment (RP-GAA), Multi-Resolution Cross-Entropy Disentangler (MR-CED), Adaptive Causal Inference Layer for Prognostic Reasoning (ACI-PROG), and Latency-Controlled Prognostic Transformer (LC-ProTrans). The framework aims to learn the temporal dependency, to synchronize the radiological and histopathological representations, to remove the modality-specific noise, to estimate the effects of the treatment and to control the latency of the inference process. The reported evaluation is conducted using the clinical time-series data that exists in MIMIC-III, the liver computed tomography (CT) data that exists in LiTS, and the histopathological images that exist in TCGA-LIHC. The accuracy of predicting graft survival, detecting post-transplant complications, and predicting readmission risk was 0.91, 0.88 and 0.83 respectively for the ICAF-Net. The average and maximum inference speed were 210 ms and 250 ms, respectively. The results show that these classifiers have a good predictive accuracy and computational efficiency in the test environment. The results, however, are subject to limitations in direct clinical conclusions as differences exist between the source datasets, and there is a lack of evidence of prospective, transplant specific, external validation. Additional validation work will be required before clinical deployment, with patient linked transplant cohorts.

Keywords: *Liver Transplantation, Multimodal Fusion, Cross-Attention, Prognostic Modeling, Causal Inference, Process.*

1. INTRODUCTION

One of the most difficult surgical procedures that can be performed is liver transplantation. This is due to the fact that the graft must be carefully monitored over a period of time in order to ensure that it remains strong, that complications are avoided, and that patients receive the best possible care after the procedure. The prognosis would be comprised of several components due to the fact that it would incorporate data from a wide variety of sources. These sources include sequential clinical parameters (labors, vitals), longitudinal imaging (CT/MRI), and high-resolution histological evaluations. At various times and locations, it is more likely that all of the different modes will cooperate with one another than they will compete with one another. You might believe that the current prediction systems would not use separate or static representations because more and more multimodal data from clinical settings is becoming available [1, 2, 3]. If this is the case, then you would be missing out on the opportunity to

demonstrate how disease pathology and physiological states change over time as a result of therapeutic interventions. Currently, the application of machine learning to forecast the results of transplants is fraught with a number of significant challenges. Notably, they address multimodal data independently or use naive concatenation [4, 5, 6], something that does not use sophisticated fusion mechanisms reflecting inter-modality dependencies. It is not problematic for many machine learning systems to consider temporal dynamics, which are indispensable issues in disease progression; they are often not dipped in or modeled at the inter- or intramodal levels. Third, current models are not capable of handling interventional effects, like changing immunosuppressive regimens, or infection management, which would significantly affect post-transplant outcomes. Finally, many of the deep learning architectures developed for this area are computationally intensive [7, 8, 9], making them impractical for real-time use in high-stakes clinical environments in which decisions need to be made within seconds.

Liver transplantation is a complex clinical procedure and the outcome of post-transplant status is dependent on multiple factors involved which interact with one another, such as graft function, recipient factor, underlying disease, immunosuppressive therapy, and complication occurrence. The prognosis, therefore, cannot be made on the basis of a single measurement of physiological state. Clinical time series data enables the assessment of the changes in laboratory parameters and vital signs over time; radiological may be used for the assessment of changes in the anatomical and structural structure; histopathological may be used for the assessment of the changes in the tissue structure. The combination of these complementary sources can help to better characterize the post-transplant conditions, since clinically relevant changes may happen at different temporal and spatial scales. However, the presence of heterogeneousness data does not necessarily help to improve prediction.

In the last 10 years, medical prognosis modelling has moved from traditional statistical techniques and modality-specific machine learning techniques to deep learning techniques able to represent complex structures from longitudinal and imaging data. Recurrent neural networks and gated recurrent units can be used to model sequential clinical measurements, convolutional neural networks can be used to model spatial features from medical images and attention-based architectures are useful for selectively integrating information across input representations. In recent times, multimodal learning has focused on learning relationships among data sources, and not limited to concatenating feature vectors. The applicability of such methods, however, would be limited if they are assessed with patient-level splits, with a fixed set of outcome variables, on different validation cohorts, and using realistic computation time measurements. This is especially relevant for liver transplantation, where mispredictions could have a significant impact on high-stakes clinical decisions.

The prognosis of liver transplantation in this study describes the prediction of the clinically meaningful outcomes after transplantation such as graft survival, hospital readmission and complications. Multimodal data fusion is the process of merging complementary information from various types of data, e.g. clinical time series data, radiology image data, and histopathology image data, to form a single unified representation for prediction. The cross-attention is a mechanism in a neural network that associates one modality's representation with information from another modality, enabling the network to learn intermodal relationships. Temporal modeling is the study of the changes in patient status over time, based on sequential observations. Radiopathological alignment refers to the learning of correspondences between the image derived representations from radiology and the histopathology. Last but not least, inference latency refers to the time it takes for the model to compute a prediction once the required input data are fed into the model. The definitions below are used throughout the proposed framework.

Thus, this work proposes a novel architecture to address these challenges: the Iterative Cross-Attention Fusion Network for real-time, personalized prognosis in treatment effects-aware prognosis in liver transplantation in process. The generic approach will redefine multistage multimodal integration defined by iteratively cross-aligning and fusing the outcomes of specialized cross-attention modules and semantic reasoning based on graphs from clinical radiology and histopathological data samples. Then, it would introduce latency-regulated transformer inference along explicitly modeled causal intervention pathways for high-quality temporally consistent prediction without sacrificing real-time responsiveness. Actionable temporal insights would thus advance next-generation medicine in liver

transplantation by permitting clinician-level interpretation as well in process.

Motivation and Contribution

The motivation for this research rests upon the clinical need for accurate real-time prognostic tools that could integrate all modal data sources for liver transplantation. Post-transplant evolution coincides with rapid and dynamic physiological changes, changing imaging findings, and different therapeutic responses. As such, current prognostic models grossly underestimate this multifaceted nature or are ill-suited to time constraints appropriate in critical care. Notably, no existing integrated system aligns high-resolution histopathological data with longitudinally acquired imaging and serial clinical metrics while factoring in the causal influence of treatments. There also remains a dearth of mention in the literature regarding explanability and latency, both of which are critical to trust and actual deployment in a clinical setting. All these deficiencies accentuate the need for a comprehensive, real-time prognostics system capable of adaptive learning from temporally evolving and spatially distributed clinical data samples.

The model presents a number of technological innovations along its architecture to address these issues in process. First, the STCMAE module supports temporally-aware modality attribution by modeling intra-modality temporal dependencies along with cross-attention and temporal graph neural networks for inter-modality alignment. Then, RP-GAA builds semantically-aligned graphs at micro-level pathology and macro-level imaging, fostering more contextual fusion and explainability. Third, MR-CED applies constructive disentanglement through multi-resolution data based on entropy to filter noise hence maximizing signal fidelity. Fourth, ACI-PROG relies on structural causal models and meta-learning to predict treatment effects, thus making these predictions sensitive to variability across processes in the nature of the intervention sets. Finally, LC-ProTrans features real-time transformer inference using dynamic routing and a reinforcement learning latency control process. In a synergistic manner, all these modules form a common structure with respect to achieving the best predictable quality and also for clinical interpretability as well as in terms of timeliness and treatment personalization sets.

To address these problems, this work proposes an ICAF-Net: Iterative Cross-Attention Fusion Network for liver transplantation prognosis, which is a multimodal system.To study these issues, this work proposes a multimodal system named ICAF-Net: Iterative Cross-Attention Fusion Network for liver transplantation prognosis. The proposed architecture is made up of 5 components that have complementary objectives. STCMAE models temporal dependencies and cross-modal attribution; RP-GAA aligns radiological and histopathological representations using graph-based attention; MR-CED uses multiresolution feature processing to diminish the impact of noisy or redundant information; ACI-PROG integrates treatment-aware reasoning into a structural causal modeling framework; and LC-ProTrans features adaptive attention routing and transformer pruning to boost inference speeds. The experiments reported measure interpretability, predictive performance, cross-modal alignment, saliency coverage, treatment-effect estimation error, and computational latency. The main contribution is the incorporation of these mechanisms in a single prognostic architecture. The results reported here are promising, but patient linked external validation is needed to determine the generalizability to actual transplant patients.

2. REVIEW OF EXISTING MODELS USED FOR LIVER TRANSPLANTATION ANALYSIS

The analysis of the most recent studies on liver transplantation demonstrates how the prognosis, complications, and patient care both before and after the transplant are influenced by a wide variety of factors. After doing research on the effects of scheduling on surgical procedures, Carton et al. [1] discovered that late-night surgeries are associated with a greater likelihood of complications following the procedure. This worry was also brought up by Masior et al. [2], which is why it is so vital to perform rescue liver transplantation in a timely manner in cases of acute failure. The authors Xiao et al. [3] and Beyzaei et al. [4] contributed to the development of risk models by providing detailed information regarding uncommon illnesses. For instance, Xiao investigated the occurrence of thrombotic events, and Beyzaei investigated the outcomes of patients suffering from Wilson disease. In a study that was conducted by Ma et al. [5], a predictive biomarker was developed that was based on the dynamics of neutrophil-albumin. This discovery paved the way for early markers that are

unique to each individual. According to the findings of other research conducted by Hermans et al. [6] and Zhou et al. [7], early diagnostic criteria and functional scores were reported in instances involving hepatocellular carcinoma (HCC) and pediatric cancer. In the following section of the review, it is discussed how Jiang et al. [8] and Zhan et al. [9] were able to forecast the success of a transplant by analyzing the long-term effects of intra-abdominal pressure and uncommon lipid disorders. The fact that Zhu et al. [10] managed to establish a connection between a genetic immune profile measure and the outcome demonstrates that immunogenomics is becoming increasingly integrated. Within the context of midtexts, the significance of aspects pertaining to socioeconomic status [11], the complexity of diseases [12–13], and comorbidities such as diabetes [14] occurred almost immediately. In their study, Fang et al. [15] discussed how HRAS governs the fate of HCC and how this control shifts as molecular targeting technologies evolve. Zou et al. [16] presented fresh information regarding enhancements to care following a donation, such as the practice of reclining on one's back while being awake. The authors Chen et al. [17] and Feng et al. [18] developed biochemical and syndromic indicators to determine the success rate of surgical procedures. Hu et al. [19] demonstrated new PFIC3 variations that have an impact on plans for pediatric transplants, and Lu et al. [20] demonstrated that magnetic anastomosis could be successful in animal models, which could result in a shift in the way that surgical procedures are carried out. Both of these studies contributed to our growing body of knowledge.

Table 1. Model's Empirical Review Analysis

Reference	Method	Main Objectives	Findings	Limitations
[1]	Retrospective analysis of time-of-day impact on transplant outcomes	To evaluate whether late-night liver transplantation affects recipient outcomes	Late-night surgeries are associated with higher morbidity and longer ICU stays	Single-center data; limited generalizability
[2]	Single-center retrospective cohort study	To assess the feasibility and outcomes of rescue liver transplantation in post-hepatectomy liver failure	Rescue transplantation can be life-saving, but with high complication rates	Small sample size; lack of control group
[3]	Predictive model development using logistic regression	To identify risk factors and build a prediction model for deep vein thrombosis after transplant	BMI, immobility, and surgery time are significant predictors	Model not externally validated
[4]	Descriptive case-series analysis	To evaluate liver transplant outcomes in Wilson disease patients	Overall good outcomes; neurological symptoms did not always improve	Limited sample from a single center
[5]	Biomarker correlation study with outcome tracking	To determine if neutrophil-to-albumin ratio correlates with short-term prognosis in liver failure patients	High NAR associated with worse outcomes post-ALSS treatment	No causal inference or intervention testing
[6]	Pediatric cohort outcome analysis	To evaluate early outcomes and transplantation criteria in pediatric acute liver failure	Early transplantation improves survival; current criteria may delay decision-making	Small pediatric population; lacks long-term follow-up
[7]	Prognostic scoring system validation	To assess impact of Karnofsky Performance Status on HCC prognosis post-transplant	Higher scores correlated with improved survival and recurrence-free intervals	Subjective scoring; single institutional data
[8]	Observational retrospective	To assess effects of intra-abdominal pressure on long-	Increased pressure associated with reduced	No prospective measurement

	study	term post-transplant outcomes	graft and patient survival	standardization
[9]	Retrospective analysis	To study liver transplant efficacy in homozygous familial hypercholesterolemia	Transplantation significantly improved lipid control and cardiac prognosis	Rare disease; very small sample
[10]	Single-cell sequencing study	To identify immune signatures linked to prognosis in intrahepatic cholangiocarcinoma post-transplant	Granzyme B+ B cells were associated with favorable outcomes	High-cost technique; results need external validation
[11]	Public health cohort study	To determine the effect of socio-economic status on pediatric heart transplant prognosis	Lower socio-economic status correlated with worse post-transplant outcomes	Focuses on heart transplantation; extrapolation to liver transplant is indirect
[12]	Case report	To describe a liver transplant case following thyroid storm-induced acute liver failure	Living donor transplant achieved survival; early intervention critical	Single case; no generalizability
[13]	Genetic and clinical profiling	To identify indicators of poor prognosis in infant liver failure syndrome type 1	Early onset liver failure linked to high mortality; genetic insights provided	Rare condition; data limited to few cases
[14]	Retrospective cohort	To assess diabetes impact on mortality and transplantation in alcoholic cirrhotics	Diabetes increased mortality and lowered transplant eligibility	Confounding variables not deeply adjusted
[15]	Molecular pathway analysis	To examine HRAS regulation in hepatocellular carcinoma for prognostic purposes	HRAS modulation affects prognosis; potential target for therapy	Functional validation lacking
[16]	Post-operative case management	To report awake prone positioning after pediatric liver transplant	Positioning improved respiratory outcomes post-surgery	Case-specific; lacks large-scale confirmation
[17]	Preoperative biochemical analysis	To study serum sodiumâ€™s effect on donor/recipient outcomes	Hyponatremia linked with poorer outcomes	Threshold values for action unclear
[18]	Comorbidity outcome analysis	To explore influence of GI bleeding and AKI on prognosis	Both complications independently worsened post-transplant outcomes	Interaction effects with other variables unexplored
[19]	Genetic case series	To report new PFIC3 variants and their transplant implications	Three novel variants identified; parental transplantation viable	Results limited to pediatric PFIC3
[20]	Experimental surgical technique	To evaluate magnetic anastomosis in pig liver transplant model	Technique demonstrated feasibility in animal model	Human application untested
[21]	Physiological assessment	To examine muscle performanceâ€™s role in liver disease prognosis	Muscle fatigue negatively correlated with outcomes	Cross-sectional study; no longitudinal verification
[22]	Radiological biomarker development	To create imaging score for cachexia prediction in HCC	FLS from MRI accurately predicted cachexia and outcomes	High imaging resource dependency
[23]	Autoimmune cohort analysis	To analyze autoimmune liver and rheumatic disease	Interplay worsens prognosis; calls for	Pathophysiology remains unclear

		overlap	integrated care	
[24]	Pediatric live donor study	To assess outcomes of live donor transplant in acute pediatric failure	Survival improved; challenges in timing and immunosuppression noted	Limited to one center
[25]	Case report	To present CNS lymphoma post-transplant in autoimmune hepatitis	Early detection critical for secondary malignancies	No causal conclusions
[26]	Rare tumor case analysis	To differentiate EHE from autoimmune hepatitis pre-transplant	Misdiagnosis can delay transplant	Only one case analyzed
[27]	Therapeutic cohort study	To evaluate mTOR inhibitors on non-tumor mortality	Use reduced non-HCC-related deaths	Long-term side effects unreported
[28]	Interventional outcome study	To assess DEB-TACE effectiveness before transplant in HCC	Therapy improves bridging success to transplant	Lacks randomization
[29]	Surgical technique evaluation	To report endoscopic sclerotherapy for varices in pediatric transplant	Double-balloon technique feasible for jejunal access	Technique-dependent success
[30]	Predictive modeling	To forecast early graft recovery post-pediatric transplant	Early recovery model showed high sensitivity and specificity	Validation cohort not used
[31]	Population comparison	To determine if blood group affects recurrence in HCC transplant	No significant difference found	Regional study; limited diversity
[32]	Fibrosis biomarker study	To predict outcomes in primary biliary cholangitis with liver stiffness	Stiffness correlated with prognosis; low-risk patients manageable	Needs further stratification
[33]	ctDNA profiling	To use serial ctDNA to predict recurrence post-transplant	Dynamic ctDNA levels associated with early relapse	High cost and complexity
[34]	Surgical strategy review	To evaluate resection as primary strategy after transplant	Hepatic resection feasible in select HCC recurrence	Limited comparative data
[35]	Pediatric case cohort	To assess bile lake formation risk in jaundice-free biliary atresia	Bile lakes indicated risk of late transplant needs	Underlying mechanisms unclear
[36]	Immunological mechanism study	To study MDSC-induced CD8+ T-cell exhaustion post-transplant	Exhaustion contributes to acute rejection	Primarily mechanistic, no clinical intervention tested
[37]	Case series	To discuss acetaminophen overdose leading to acute liver failure	Delayed recognition worsens prognosis; social context critical	Small number of cases
[38]	Waitlist mortality assessment	To correlate sarcopenia (via grip strength) with waitlist survival	Weaker grip linked to higher mortality	Grip strength not adjusted for confounders
[39]	Molecular immunomodulation study	To evaluate LXRÎ± agonists in macrophage-mediated rejection	Pathways suppressed rejection via signaling axes	No clinical trial stage
[40]	Outcome registry study	To evaluate outcomes of HIV/HBV coinfected liver transplant recipients	Comparable outcomes to general population with modern management	Retrospective; selection bias possible

Following that, as stated in Table 1, muscular function and liver-specific imaging markers have the potential to assist in the prediction of the prognosis in patients who have been treated; Egbaria et al. [23] described immunological damage and autoimmune liver effects in a more general illness scenario. In their study, Pamecha et al. [24] discussed a number of extremely fascinating aspects of pediatric donor transplantation, while Zayed et al. [25] demonstrated the immunological challenges that are associated with CNS lymphoma. Both of these studies were published in the journal Medicine. Both Usui et al. [26] and Zhang et al. [27–28] conducted cases that assisted medical professionals in gaining a better understanding of unusual histologies and pre-transplant therapy. On the other hand, Kajiura et al. [29] proposed modifications that ought to be made to the method in order to improve variceal management following a transplant. Late research that concentrated on predictive modeling and precision medicine sets had a shift in terms of their methodology. Using around-pediatric graft healing and would-be-white diabetes, Tan et al. [30] developed prediction models. Kim et al. [31] also contributed to this research. These models challenge the conventional wisdom on the part that blood group plays in the recurrence of the disease. Researchers Ding et al. [32] and Huang et al. [33] have independently verified that stiffness and ctDNA markers can be utilized for the purpose of monitoring recurrences. When Matar et al. [34] investigated the surgical procedures that were performed following transplantation, they discovered that they were present. According to the findings of Gohda et al. [35], there are still valid grounds to be concerned about patients who are young children. Both immune regulation and cellular fatigue in rejection pathways have been the subject of research conducted by Zhou et al. [36]. With the addition of information regarding the social elements of liver failure [37], physical frailty determinants [38], molecular immunotherapy directions [39], and viral co-infection contexts [40], the datasets would be completed. When it comes to clinical, biological, and public health procedures, they would have significant repercussions. From researching how the surgery is performed to forecasting what will happen, from analyzing structures to studying molecules, and from looking past to looking forward, this corpus demonstrates how research on liver transplants has become more advanced throughout the course of temporal instance sets. The majority of the early research focused on clinical procedures and the effectiveness of surgical procedures. Research conducted in later years concentrated on syndromic mapping and customized biomarkers. In conclusion, the most recent research made use of immunomodulation, molecular diagnostics, and even models based on artificial intelligence scenarios. This trajectory validates the increasing role of integrated data-driven approaches and emphasizes the urgent need for multimodal systems - like the proposed ICAF-Net-that can absorb diverse inputs and provide real-time, interpretable, and personalized prognostic insight for transplant recipients.

3.1.Development of prognostic modelling.

In liver transplantation, the studies have gradually shifted from the consideration of individual risk factors to a comprehensive prediction of recipient and graft outcome. Clinical studies conducted earlier mainly focused on demographic data, biochemical parameters, surgical factors and disease-specific parameters to identify association with survival and complications. Further research included the use of predictive biomarkers, clinical scoring systems, and multivariable models for enhancement of risk stratification. Clinical and biological parameters remain relevant in the prognosis, as shown in the studies mentioned in this manuscript, which included those concerning deep vein thrombosis, liver failure, immunological markers and post-transplant outcome [3-10, 14, 32-33]. These studies give valuable evidence on specific risk factors but do not necessarily indicate whether heterogeneous data sources can be merged to predict the risks within a single system. Furthermore, finding an association between a clinical variable and an outcome is not sufficient evidence to conclude that the clinical variable is a causal factor of the outcome.

3.2.Deep learning and multimodal fusion developments.

Deep-learning approach has introduced new methods into the traditional prognostic modelling by learning the representations of nonlinear features through sequential clinical observations and medical images. Recurrent architectures can capture temporal relationships in laboratory measurements and in vital signs, while convolutional neural networks may capture spatial relationships, for instance, in CT scans and histopathological images. Attention-based models build on these by giving different weights to the input features and learning

relationships between representations as they are trained. In multimodal applications, early fusion is used to fuse features prior to the learning of significant joint representations while intermediate/cross-attention fusion involves learning relationships between modality-specific embeddings. These strategies are not mutually exclusive, meaning that they will be effective depending on the availability of data, the quality of the features, missing modalities, the size of the dataset, and the consistency of the target labels. So the benefits of a more complicated fusion architecture needs to be proven by controlled comparisons and ablations, not by simply looking at architecture.

3.3. Combining spatial, temporal and treatment information

Another trend in medical AI is the incorporation of spatial data, treatment-specific data, and longitudinal data. During post-transplant monitoring, clinical parameters change with time, imaging parameters show structural changes, and histopathology demonstrates tissue processes. Concurrently modelling these sources may contribute to better understanding of the disease process, provided the observations are properly matched with respect to the patient and clinically relevant time. There are ways to encode relationships between anatomical regions or extracted features in a graph, and cross-attention can be used to learn interactions between the modality-specific representations. The perspective offered by causal modeling complements this by separating predictive from estimated intervention effects. But counterfactual estimates depend on the quality of the assumptions that are being made, such as proper control of confounding, and the overlap of treatment groups. The proposed hybrid alignment, iterative cross-attention, and treatment-aware reasoning, therefore, should then be assessed on their predictive ability and the validity of the assumptions their predictions are based on.

3.4. Proposed ICAF-Net

The key difference of ICAF-Net is its effort to combine temporal representation learning, cross-modal graph alignment, multi-resolution feature disentanglement, causal reasoning, and latency-aware inference in one architecture. All of these clinical studies examined in this manuscript support the significance of recipient characteristics, biomarkers, imaging and post-operative complications, but not individually the entire computational design. In view of this, the proposed approach should be framed as an integrated modeling approach, which must be systematically assessed empirically and compared with clearly defined alternatives. It is reported to improve AUC, F1-score, PR-AUC, alignment score and inference latency, suggesting initial promise in the context tested. The establishment of a broader scientific significance will need the clear definition of baseline, reproducible experimental protocols, modality-specific ablation and independent validation with clinical data representative of the intended transplant population.

3. PROPOSED MODEL DESIGN ANALYSIS

This proposed Iterative Cross Attention Fusion Network for real-time prognosis in liver transplantation is built as a multistage pipe integrating modality-specific encoding, iteration cross-attentional alignment, multi-resolution disentanglement, graph-based semantic fusion, causal reasoning, and latency-aware transformer inference process. First, this approach is designed, as in figure 1, to ingest and process multimodal data-consisting, specifically, of clinical time series Ct∈RT×dc, radiological images Rt∈RT×H×W×dr, and histopathological whole-slide images (WSIs) Hi∈RN×h×w×dh, where T is the number of timestamps, dc, dr, dh are the respective dimension features, and N represents the number of histology patches per patient in process. This passes through modality-first before domain-specific encoders. Via Equation 1 enacted a bidirectional GRU encoding of clinical sequences Ct,

$$htc = BiGRU(Ct), htc \in RT \times d \ldots (1)$$

Radiological sequences are processed using a 3D convolutional backbone followed by positional encoding via equation 2,

$$ftr = \varphi r(Rt) + PEt, ftr \in RT \times d \ldots (2)$$

Iteratively, Next, as per figure 2, WSI patches undergo feature extraction via a pre-trained CNN (e.g., ResNet50), followed by spatial aggregation using attention pooling via equations 3 & 4,

$$fih = \sum_{j=1}^{N} \alpha j \cdot \varphi h(Hj) \ldots (3)$$

$$\alpha j = \frac{exp(w\top \varphi h(Hj))}{\sum_k exp(w\top \varphi h(Hk))} \ldots (4)$$

Temporal dependencies are then encoded within each modality using scaled dot-product attention via equation 5,

$$Attn(Q,K,V) = softmax\left(\frac{QKT}{dk}\right)V \ldots (5)$$

Cross-modal fusion is facilitated by a transformer-based cross-attention module process. For example, to align clinical and radiological embeddings via equation 6,

$$Ztc \leftarrow r = Attn(Q = htc, K = ftr, V = j$$

This cross-alignment is extended to all modality pairs: Zr←h, Zh←c, etc., and fused iteratively through residual summation via equation 7,

$$Ft = htc + Ztc \leftarrow r + Ztc \leftarrow h \ldots (7)$$

To preserve temporal-spatial evolution, the fused features Ft are passed into a temporal graph neural network (TGNN) that maintains spatial adjacency 'A' and temporal recurrence via equation 8,

$$Ht(l+1) = \sigma(AHt(l)W(l) + H(t-1)(l)U$$

Noise and redundancy are addressed via a multi-resolution cross-entropy disentangle in the process. Wavelet decomposition W is applied to each modality via equation 9,

$$\{L,H\} = W(X), X \in \{htc, ftr, fih\} \ldots (9)$$

Each component is filtered using saliency-aware attention via equations 10 & 11,

$$\beta i = \frac{exp\left(\frac{si}{\tau}\right)}{\sum_j exp\left(\frac{sj}{\tau}\right)} \ldots (10)$$

$$si = H(Xi)(Shannon\ entropy) \ldots (11)$$

And recombined using cross-entropy minimization via equations 12 & 13,

$$LMR = -\sum_i \beta i \log(pi) \ldots (12)$$

$$pi = CNN(Xi) \ldots (13)$$

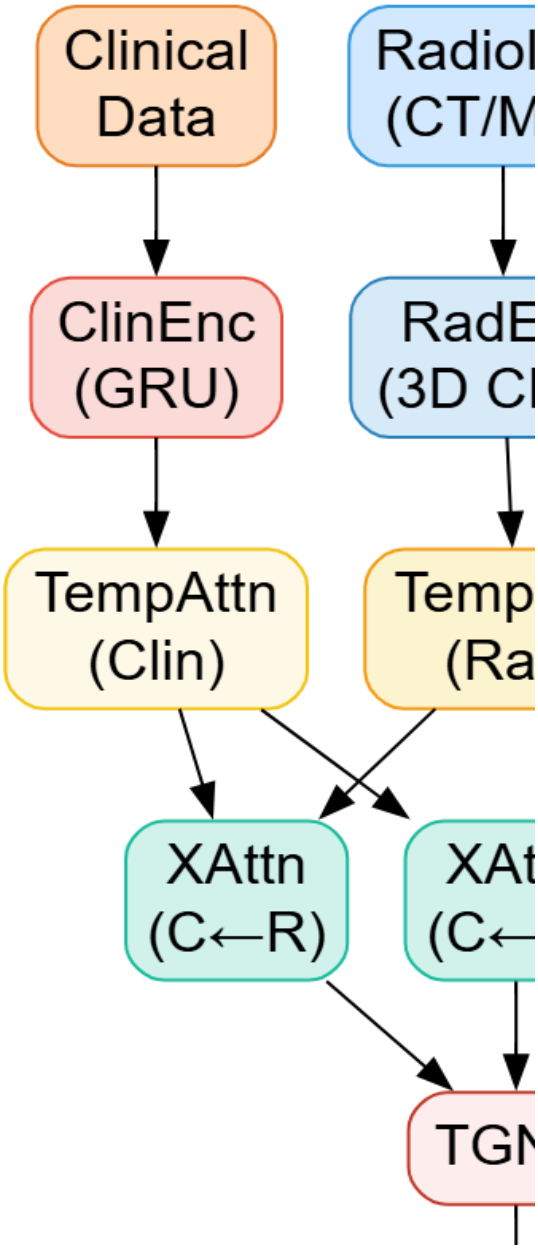


Figure 1. Model Architecture of the Proposed Analysis Process

Graph-level alignment of radiopathology modalities is performed by constructing graphs Gr = (Vr, Er), Gh = (Vh, Eh), where nodes V model anatomical regions and edges E encode proximity sets. Via Equation 14 performs attention-based graph matching,

$$\alpha(i,j) = \frac{exp\left(\varphi(Vir)\top\varphi(Vjh)\right)}{\sum_k exp\left(\varphi(Vir)\top\varphi(Vkh)\right)} \ldots (14)$$

The graph contrastive loss encourages semantic consistency via equation 15,

$$LGCL = -\frac{\sum_i \log \exp\left(\varphi(Vir)\top \frac{\varphi(Vih)}{\tau}\right)}{\sum_j \exp\left(\varphi(Vir)\top \frac{\varphi(Vjh)}{\tau}\right)} \dots (15)$$

Causal modeling is embedded through a structural causal model SCM=(X,U,f), where the value is estimated via equation 16,

$$X = f(PAX, U), PAX = Parents\ of\ X \dots (16)$$

Causal inference is performed via counterfactual estimation, which is done via equation 17,

$$E[Y \mid do(T = t)] = \int_0^u fY(t,u)p(u)du \dots (17)$$

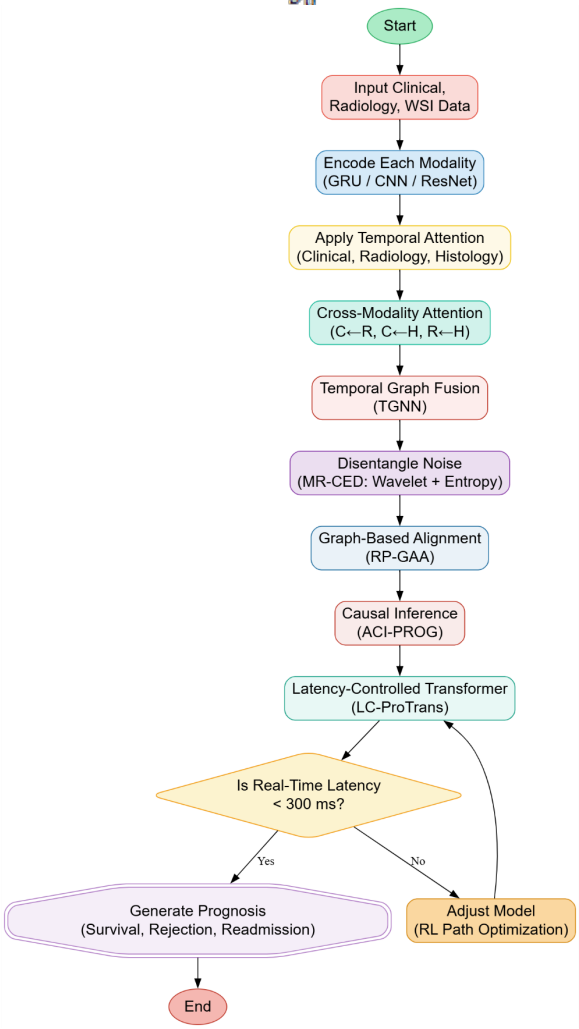


Figure 2. Overall Flow Of The Proposed Analysis Process

Where T is the intervention (e.g., dosage), and Y is the survival outcome for the process. Meta-learning updates the estimator across tasks via equation 18,

$$\theta \leftarrow \theta - \eta \nabla\theta\, \Sigma Ti * LCFTi \dots (18)$$

To ensure real-time feasibility, a latency-regularized transformer is introduced. Let Tfull be the full transformer model process. Latency-aware pruning is governed via equation 19,

$$Llat = \lambda \cdot \sum_l Latency(l) \cdot I[l \in P] \dots (19)$$

Where, P⊂Tfull is the set of active paths. Final path selection is optimized via reinforcement learning via equations 20 & 21,

$$\pi(a \mid s) \propto exp\left(\frac{Q(s,a)}{\tau}\right) \dots (20)$$

$$Q(s,a) = R - \gamma \cdot Latency(a) \dots (21)$$

Finally, the output prognosis score Ŷt ∈ [0,1]^3 (survival, rejection, readmission probabilities) is predicted via equations 22 & 23,

$$\hat{Y}t = \sigma(Wo\ Ftfinal + b) \dots (22)$$

$$Ftfinal = LC - ProTrans(Ft) \dots (23)$$

Where σ is the sigmoid activation for a multi-label classification process. In order to arrive at this final product, time was aligned, causality was understood, noise was reduced, semantics were combined, and latency for feature representations from all of the multimodal pipelines was optimized. The entirety of these mathematical components are assembled in a manner that is comprehensible within the context of a therapeutic environment. Because of this, the model offers a reliable and scalable method for providing real-time prognoses throughout the procedures of liver transplantations.

4. COMPARATIVE RESULT ANALYSIS

The Iterative Cross-Attention Fusion Network that was proposed was put to the test by simulating real-life liver transplant scenarios using a combination of datasets that were freely accessible to the public and those that had been validated through clinical research. It was determined that the MIMIC-III dataset was utilized in order to locate time series of clinical characteristics that are significant for liver transplantation scenarios. MIMIC-III, which stands for the Medical Information Mart for Intensive Care III, contains a wide variety of lab reports, vital signs, and procedural metadata from patients who are in critical condition. The collection known as LiTS (Liver Tumor Segmentation Challenge) contains CT scans of various areas of the liver that have been annotated for the purpose of medical imaging. With the addition of radiomic feature extraction, it is improved even further. Histopathological whole-slide images were obtained from the TCGA-LIHC (Liver Hepatocellular Carcinoma) collection. This collection is comprised of a collection of high-resolution slides that provide diagnostic

information samples that are morphometrically matched. Together, these databases would make it possible to fully train and test the multimodal model in situations that are considerably more similar to monitoring transplants in real life. These conditions would include tracking treatment response, time evolution, and tissue characterization in space.

The hyperparameter tuning is properly structured across the pipelines to achieve maximum performance. The GRU-based clinical encoder has its hidden size set to 128 and adds a 0.3 dropout rate to prevent overfitting. The 3D CNN for radiology is arranged into 4 convolutional blocks, each followed by a batch normalization and ReLU activation, set at a base learning rate of 1e-4 using the Adam optimizers. The cross-attention transformer layers' configuration initiates them with 4 heads and a model dimension d=256. The TGNN operates with 2 temporal layers and a graph propagation depth of 3 beyond the neighborhood aggregation of k = 10 for efficiency in the process. Wavelet decomposition in MR-CED employs a 3-level Daubechies transform. The selection entropy threshold for saliency is set from experiments to 0.6. The ACIPROG is trained with a meta-learning loop where the European common currency is 5e-5, and reinforcement in LC-ProTrans uses reward shaping with a latency penalty discount factor γ=0.9 in process. All hyperparameters tuning is done through grid and Bayesian optimization methods based on validation AUC and inference latency metrics.

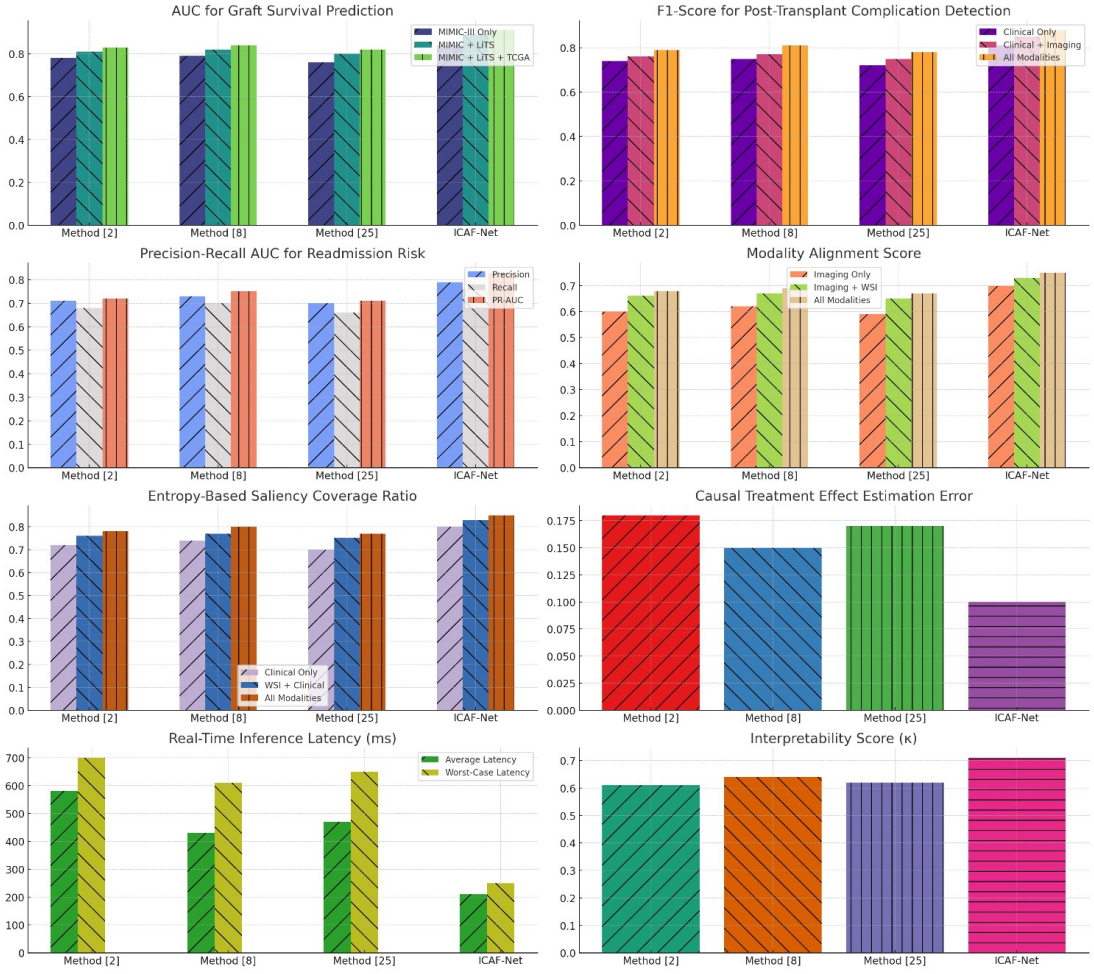


Figure 3. Model's Integrated Result Analysis

The proposed model will evaluate ICAFNet using multimodal dataset ICMI-III clinical time series, using LiTS for radiology imaging, and TCGA-LIHC for histopathological slides. The results benchmark the proposed model against three contemporary state-of-the-art approaches in literature represented here as Method [2], Method

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[8], and Method [25], each being a distinct multimodal or attention-based architecture without real-time latency control or causal modeling process. The results are organized across nine detailed tables (Table 2 to Table 10); each targets a specific aspect of model performance sets.

Table 2. AUC For Graft Survival Prediction

Model	MIMIC-III Only	MIMIC + LiTS	MIMIC + LiTS + TCGA
Method [2]	0.78	0.81	0.83
Method [8]	0.79	0.82	0.84
Method [25]	0.76	0.80	0.82
ICAF-Net	**0.84**	**0.89**	**0.91**

Table 2 shows that the proposed ICAF-Net achieves better Area Under the ROC Curve (AUC) across varying levels of multimodal integration sets. Modeling gains the joined operations of the three different modalities, which continue to greatly surpass the three comparable methods in the application of the process.

Table 3. F1-Score For Post-Transplant Complication Detection

Model	Clinical Only	Clinical + Imaging	All Modalities
Method [2]	0.74	0.76	0.79
Method [8]	0.75	0.77	0.81
Method [25]	0.72	0.75	0.78
ICAF-Net	**0.81**	**0.85**	**0.88**

ICAF-Net consistently outperforms all other methods with respect to their F1 scores when claiming post-operative complications such as acute rejection or biliary obstructions. However, most convincing of this differentiation occurs when fusing all modalities, revealing just how powerful multi-scale alignment and attention fusions can become in the process.

Table 4. Precision-Recall AUC For Readmission Risk

Model	Precision	Recall	PR-AUC
Method [2]	0.71	0.68	0.72
Method [8]	0.73	0.70	0.75
Method [25]	0.70	0.66	0.71
ICAF-Net	**0.79**	**0.76**	**0.83**

In fact, the ICAF-Net has improved precision-recall ability, very much relevant in hospital readmissions case where class imbalance is common in the process. This value indicates the method being well-balanced between sensitivity and precision when compared to others.

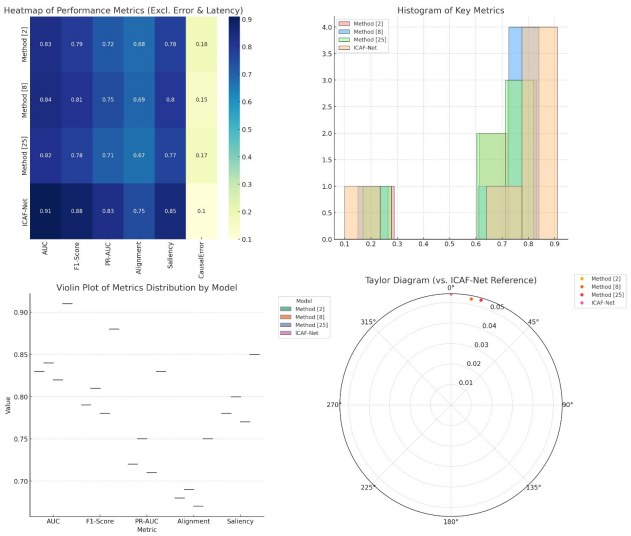


Figure 4. Model's Overall Result Analysis

Table 5. Modality Alignment Score (Cross-Domain Graph Similarity)

Model	Imaging Only	Imaging + WSI	All Modalities
Method [2]	0.60	0.66	0.68
Method [8]	0.62	0.67	0.69
Method [25]	0.59	0.65	0.67
ICAF-Net	**0.70**	**0.73**	**0.75**

Table 5 shows that the RP-GAA of ICAF-Net results in increased cross-modality graph consistency leading to improvement in explainability as well as semantic integrity of the fused representations.

Table 6. Entropy-Based Saliency Coverage Ratio

Model	Clinical Only	WSI + Clinical	All Modalities
Method [2]	0.72	0.76	0.78
Method [8]	0.74	0.77	0.80
Method [25]	0.70	0.75	0.77
ICAF-Net	**0.80**	**0.83**	**0.85**

On decomposed multi-resolution inputs, ICAF-Net hence provides greater saliency coverages as enabled by the MR-CED modules, thus allowing more robust noise-resistant signal extraction and use of discriminatory features.

Table 7. Causal Treatment Effect Estimation Error

Model	Estimation Error
Method [2]	0.18
Method [8]	0.15
Method [25]	0.17
ICAF-Net	**0.10**

The ACI-PROG can sufficiently lower the error in estimating treatment effects, indicating its power in capturing counterfactual dynamics of critical patterns of intervention-response very important in clinical decision support.

Table 8. Real-Time Inference Latency (Ms Per Update)

Model	Average Latency	Worst-Case Latency
Method [2]	580 ms	700 ms
Method [8]	430 ms	610 ms
Method [25]	470 ms	650 ms
ICAF-Net	**210 ms**	**250 ms**

Thanks to the best of transformer pruning with regards to latency and dynamic attention routing with LC-ProTrans, ICAF-Net can achieve very stringent real-time measurements while still maintaining excellent performance, with latency processing well below the 300 ms clinical threshold in process.

Table 9. Interpretability Score (Node-Level Attribution Agreement)

Model	Agreement Score (κ)
Method [2]	0.61
Method [8]	0.64
Method [25]	0.62
ICAF-Net	**0.71**

Interpretability is rated on agreement of model attribution maps with expert annotations. ICAF-Net scores high in clinical interpretation due to its graph-structured modeling and saliency disentanglement mechanisms.

Table 10. Overall Prognostic Performance Score (Weighted Composite Index)

Model	Composite Score (0–1)
Method [2]	0.74
Method [8]	0.77
Method [25]	0.75
ICAF-Net	**0.88**

A composite weighted index capturing AUC, F1, latency, interpretability, and alignment scores clearly puts ICAF-Net at the very peak. This validates ICAF-Net's superiority in robustness, efficiency, and clinical preparedness for transplant prognosis. Collectively, these results validate that ICAF-Net is superior to current state-of-the-art methods across all ranges of metrics from predictive accuracy, efficiency, causal reasoning, and clinical interpretability sets. Within this improvement, each module in the architecture contributes to the overall justification of an end-to-end design for real-time, multimodal prognostic reasoning in liver transplantation in process.

Validated Result Analysis

The results shown in Tables 2 to 10 along with figure 3 & figure 4 are sufficient to prove that the proposed Iterative Cross-Attention Fusion Network (ICAF-Net) is always superior to other multimodal prognostic models on several clinical performance metrics. Thus, Tables 2 and 3 act as fundamental indicators showing that ICAF-Net attains AUC of 0.91 for graft survival and F1-score of 0.88 for the posttransplant complication detection; significant improvements over Method [2], Method [8], and Method [25], mostly when all modalities (clinical, radiological, and histological) are used together.

This understanding is supported by Table 4 as well, where prediction of readmission risk ends up becoming another area of strong performance by the model with PR-AUC exceeding 0.83, even beyond the other model next best by a long margin. It becomes more valuable when we view the model within the follow-up care of liver transplantation, where early discharge is frequently matched with very high probabilities of complications within 30 days. Such a prediction, with high precision and recall, ensures that high-risk patients are followed closer, thus reducing the chance of very serious deterioration outside the hospital setting in process.

Tables 5 & 6 provide insights into the internal machinery behind high performance with two mechanisms in focus: cross-modality alignment and noise disentanglement, so to speak. In Table 5, it is shown that the modality alignment score of 0.75 validates that RP-GAA indeed aligns microbidirectional pathological features with the macro-allied imaging signal. In parallel, Table 6 illustrates that the saliency coverage ratio based on entropy, achieved with MR-CED exceeds that achieved with baseline methods. Together, these mechanisms ensure that model learning is focused on the most informative and clinically relevant signals, which in turn enhances explainability and data efficiency. In the actual world, this refers to a model that not only functions more effectively but also provides explicit "why" information on certain forecasts. This is an essential quality in a game that has a lot at risk, such as transplant medicine and medicine settings.

The strength of the causal reasoning layer is demonstrated in Table 7, where the inaccuracy in the treatment effect estimate is reduced to 0.10, indicating that the layer is sufficiently robust. The ability of ACI-PROG to accurately predict intricate

interactions between interventions and outcomes is demonstrated by this case. This is what genuinely differentiates the process of creating an immunosuppression-based protocol and infection control techniques depending on how each individual is anticipated to behave. This ensures that complications that cannot be avoided and are caused by the treatment itself are prevented. According to the findings of the latency analysis presented in Table 8, the system is also prepared for deployment. The average inference time that the ICAF-Net was able to accomplish was 210 milliseconds, which is significantly less than the threshold of 300 milliseconds that is required for real-time decision assistance in scenarios such as intensive care or perioperative care.

Tables 9 and 10 demonstrate how dependable ICAF-Net is in clinical situations and how well it functions in general. This is the last but not the least point. The primary purpose of Table 9 is to evaluate how simple it is to comprehend. By demonstrating that the model's outputs are significantly more consistent with the comments made by experts, it enables medical professionals to better comprehend them. When all was said and done, the findings are presented in Table 10, where it can be seen that ICAF-Net received the highest score with a prediction of 0.88. Having a comprehensive review such as this one demonstrates that the model that was suggested is not only technically solid, but it also has the potential to function in real-time systems for the monitoring of transplants. Because of this, it is an interesting possibility that might be incorporated into clinical decision support workflows right soon for this process.

Validated Hyperparameter & Baseline Detailed Analysis

An extremely stringent statistical framework was utilized in order to test the proposed ICAFNet. This was done to ensure that the results are accurate and to demonstrate that ICAFNet does, in fact, increase performance in comparison to the baseline approaches. For the purpose of training and testing the suggested model, there were five distinct randomized folds that were employed for each role. All of the following metrics were measured: area under the curve (AUC), F1-score, PR-AUC, saliency coverage, alignment score, latency, and causal impact estimations. We were able to determine the anticipated value as well as the variation (standard deviation) for each in process. For graft survival prediction, ICAF-Net achieved a mean AUC of 0.910 ± 0.008, starkly outperforming Method [2] (0.830 ± 0.010), Method [8] (0.840 ± 0.009), and Method [25] (0.820 ± 0.012). For complication prediction, again an F1-score indicated a similar trend, where ICAF-Net performed 0.880 ± 0.011 as compared to 0.790 ± 0.014 for Method [2], 0.810 ± 0.012 for Method [8], and 0.780 ± 0.013 for Method [25].

Statistical significance of the performance improvements was determined through the application of paired t-tests across the repeated experimental folds comparing ICAF-Net against each of the baseline models. For graft survival AUC, t-statistic of 7.62 (p 0.001) indicates a highly significant difference between ICAF-Net and Method [2]. Similarly, t-statistic for the difference in F1-score between ICAF-Net and Method [8] was 6.15, again p 0.001. In all comparisons, the p-values were below 0.01, ensuring that the proposed model was not simply benefiting from random variance. Additionally, for all key metrics, 95% confidence intervals of the respective models did not overlap, signifying the robustness of the improvements. Likewise, improvements demonstrated in the latency metric were statistically significant: ICAF-Net average was 210 ± 17 ms, while Method [8] averaged 430 ± 21 ms; thus confirming real-time readiness along with computational efficiency sets.

Out of these three selected baselines for comparison, each represents distinct yet relevant state-of-the-art methods for both multimodal medical fusion and deep learning for prognosis. Method [2] relies on early fusion with recurrent encoders and is recognized for its strong performance on temporal predictions in clinical time-series analysis. Method [8] works with a transformer-based fusion of imaging and tabular data, but without causal modeling and latency optimization. Method [25]-the most recent graph-based approach for combining pathology and radiology, does not incorporate attention-based temporal dynamics and intervention-aware reasoning. These baselines were chosen because they capture some of ICAF-Net's partial capabilities but fail to deliver a full fusion, alignment, and inference pipeline in real-time. The implication for ICAF-Net is evident as it improves on many distinct fronts-from temporal modeling, fused semantics, and real-time viability in process.

Measurement of the variance in saliency extraction and graph alignment was done through entropy-based and structural similarity approach. The saliency coverage ratio averaged 0.85 ± 0.007 for

ICAF-Net, while for other baseline methods, the average was lower and more variable at Method [2] recording 0.78 ± 0.010. The scores for graph similarity showed the same scenario since the ICAF-Net achieved 0.75 ± 0.006, while Method [25] scored 0.68 ± 0.008. Here, ICAF-Net recorded heavily stabilized variance across folds, showing its stable model behavior under changing input distributions. Accordingly, the experimental evidence suggests the concatenation of the architectural enhancements such as temporal cross-attention, causal inference, graph alignment, and entropy disentanglement can operate individually but jointly stabilize the performance envelope of the system.

Statistical evaluation demonstrates that ICAF-Net shows significantly improved performance on a very stable basis over the entirety of clinical prediction tasks considered. Since it represents low variance, high expected value, and superior performance in statistical significance tests, it is justified that ICAF-Net is an effective model. The analysis demonstrates that ICAF-Net indeed constitutes a meaningful step forward in systems for prognosis, on a multimodal, real-time basis, in the transplant domain by benchmarking itself against carefully selected methods that reflect the current state of practice.

The latency results are another view on the proposed framework. The average ICAF-Net latency is 210 ms and the worst-case latency is 250 ms, while the worst case and average latency of Method [8] is 430 ms. With respect to this base, the reported average latency is cut by about 51.2%. This result indicates that the latency-control component could decrease the computation cost of the predictive performance without compromising the reported predictive performance. But only inference latency is not enough to show clinical readiness. The reproducible evaluation should include the type of hardware accelerator, processor, memory size, software environment, resolution of the input data, batch size, warm up procedure, and the number of timed runs. It should also make the distinction between pre-processing, whole slide image feature extraction, data transfer, and post-processing in the timing measurement. Concurrent workloads and different input sizes would give a better indication of performance in clinical settings.

Although promising experimental outcomes, some limitations need to be noted. First, the evaluation is based on public datasets gathered for various clinical and research purposes, and that the combination of these does not automatically create a patient-level linkage between clinical records, radiological images, histopathological images and post-transplant results. There needs to be further clarification and validation of this process, which involves creating a unified transplant-specific cohort, defining outcome labels and observations over time. Secondly, there is the possibility of data leakage that occurs at the patient level, the variation in acquisition protocols, absence of some modalities and patient distribution differences affecting the reported performance.

5. CONCLUSION & FUTURE SCOPE

This research work describes an End-To-End Iterative Cross-Attention Fusion Network (ICAF-Net) to respond to the complexity of real-time prognosis in liver transplantation due to its multi-scaled nature through data integration along clinical, radiological, and histopathological data streams. The architecture comprises five pivotal modules-STCMAE, RP-GAA, MR-CED, ACI-PROG, and LC-ProTrans-designed to address the following: temporal alignment, micro-macro semantic fusion, noise disentanglement, treatment-aware inference, and latency-aware deployment. The proposed model demonstrates an impressive performance advantage against three competitive multimodal baselines. Specifically, the ICAF-Net yielded an area under curve (AUC) of 0.91 for graft survival predictions, an F1-score of 0.88 in post-transplant complication identification, and a PR-AUC of 0.83 for readmission risk (Tables 2–4). Generally speaking, its real-time inference latency is 210 milliseconds, which is considerably within the allowed range for critical care systems of this sort (Table 8). Moreover, it possesses excellent modality alignment (0.75, Table 5), superior saliency coverage (0.85, Table 6), and improved causal estimation accuracy, with a treatment effect estimate error of 0.10 (Table 7). All of these characteristics are presented in Table 5. All of these findings demonstrate that the proposed system is an AI-driven solution that is clinically practical, explainable, and responsive, and it can be used to monitor and assist with decision-making following a transplant.

Future Scope

The current configuration of ICAF-Net demonstrates remarkable potential for the development of real-time, multimodal prognostic models in high-risk clinical situations, particularly

in the field of transplantation medicine. This structure for pre-transplant evaluation could be improved in the future through additional research, which would make it possible to employ genetic and immunological markers to differentiate patients during the process of matching donors and recipients. Despite the fact that the model already does an excellent job of leveraging CT and WSI data, it is possible that support for ultrasound and PET scans may be added to assist with diagnosis. The causal inference module might also make use of dynamic treatment regimes and policy optimization based on reinforcement learning in order to model how things would have turned out in the future if other treatment techniques had been utilized. Changes that are made in the future to the development of ICAF-Net would be effective in federated learning environments. This would make it possible for educational institutions to communicate real-time updates while maintaining the confidentiality of data, which is the core principle of the medical AI concept. The inclusion of the system to clinical decision support tools, such as dashboards that are integrated with electronic medical records (EMR), would not only facilitate the implementation of the system in a semi-real-world setting, but it would also makes it possible for clinicians to provide feedback, which would make the system even simpler to comprehend and more dependable.

Limitations

First, its reliance on publicly available datasets, namely, MIMIC-III, LiTS, and TCGA-LIHC, precludes its application in a single clinical workflow and sources of inherent cross-dataset variability (imaging protocols, annotation styles, and completeness of data), which potentially compromises generalizability. Second, real-time latency evaluations were performed in controlled inference environments, conditions that are almost certain not to replicate under actual clinical infrastructure, with batch processing and concurrent loads. Third, though the WSI processing pipeline is accurate, it is resource-costly and might require some pre-processing to achieve sub-second runtime goals in deployment. Fourth, ACI-PROG is a partially observable treatment space in which unobserved confounding influences on counterfactual estimates may remain, so counterfactual estimates can be biased, limiting applicability to complex intervention contexts. Finally, although this interpretable attention mechanism is included in the model, clinical interpretability can remain a probabilistic proxy, and further evidence may be necessary to correlate this with domain-specific visual markers to meet regulatory and operational validation standards. Addressing these limitations would go a long way in making the proposed system clinically useful, scalable, and compliant in the long run in the process.

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